CLEARANCE RATE COMPARISON IN SECOND LOOK NEPHROSCOPY VS PCNL ALONE FOR STONES LESS THAN 800 HOUNSFIELD UNITS. A RANDOMISED CONTROL TRIAL IN HOSPITAL TENGKU AMPUAN AFZAN, KUANTAN, MALAYSIA

BY

SYAFIQ HUSNI BIN MOHD MURAD

A dissertation submitted in fulfilment of the requirement for the degree of Master of Surgery (General Surgery)

Kulliyyah of Medicine

International Islamic University Malaysia

JANUARY 2018

ABSTRACT

Residual stones post percutaneous nephrolithotomy (PCNL) are not detected up to 17% on post-operative imaging. Plain radiograph may not detect residual for radiolucent or vague radio opaque stones post-operatively. Our objectives was to determine the incidence of significant residual stones of less than 800HU and whether routine second look nephroscopy improves the clearance rate of PCNL. We conducted a prospective single center randomized control trial from June 2015 to December 2017 in Hospital Tengku Ampuan Afzan, Kuantan, Malaysia, comparing PCNL only with PCNL with second look nephroscopy for stones less than 800HU. Patients were randomized to "PCNL only" or "PCNL with second look nephroscopy". Both arms are followed up at 3 months with ultrasonography to detect residual. The primary end point was clearance rate of PCNL with second look compared to PCNL only. All enrolled patients, 60 were comparable for age ($p = 0.517$), gender ($p = 0.305$), BMI ($p = 0.036$) and ASA ($p = 0.456$). Between two groups, mean Hounsfield Unit (HU) were 472 ($p = 0.794$), duration of op ($p = 0.193$), and stone size ($p = 0.053$). At initial, clearance rate of PCNL alone is 80% vs 70% for second look group. Post-operative KUB X-ray detected additional 2 patients in residual in PCNL only group and 5 in the Second Look group. The intervention group (second look nephroscopy) was able to detect 40% more residual stones by which 43% were cleared, the rest were not cleared due to intervention failure and unreachability. Post-operative ultrasound showed residuals in 3 patients who received second look compared with 15 residuals detected on PCNL only, a difference of 58% vs 89% respectively which is statistically significant ($p = 0.002$; < 0.05). Second look nephroscopy is able to detect missed radiolucent stones post PCNL up to 40% and improve clearance rate of radiolucent stones up to 90% compared to PCNL alone.

APPROVAL PAGE

I certify that I have supervised and read this study and that in my opinion; it conforms to acceptable standards of scholarly presentation and is fully adequate, in scope and quality, as a dissertation for the degree of Master of Surgery (General Surgery)

……..

Islah Munjih Ab Rashid
Supervisor

……..

Abdul Hamid Bin Ghazali
Co-Supervisor

I certify that I have read this study and that in my opinion it conforms to acceptable standards of scholarly presentation and is fully adequate, in scope and quality, as a dissertation for the degree of Master of Surgery (General Surgery)

……..

Nasser Mohammad Amjad
Examiner

This dissertation was submitted to the Department of Surgery and is accepted as a fulfilment of the requirement for the degree of Master of Surgery (General Surgery)

……..

Junaini Kasian
Head, Department of Surgery

This dissertation was submitted to the Kulliyyah of Medicine and is accepted as a fulfilment of the requirement for the degree of Master of Surgery (General Surgery)

……..

Azmi Md Nor
Dean, Kulliyyah of Medicine

DECLARATION

I hereby declared that this dissertation is the result of my own investigations, except where otherwise stated. I also declare that it has not been previously or concurrently submitted as a whole for any other degrees at IIUM or other constitutions.

Syafiq Husni Bin Mohd Murad

Signature:…….. Date:…….

INTERNATIONAL ISLAMIC UNIVERSITY MALAYSIA

DECLARATION OF COPYRIGHT AND AFFIRMATION OF FAIR USE OF UNPUBLISHED RESEARCH

CLEARANCE RATE COMPARISON IN SECOND LOOK NEPHROSCOPY VS PCNL ALONE FOR STONES LESS THAN 800 HOUNSFIELD UNITS. A RANDOMISED CONTROL TRIAL IN HOSPITAL TENGKU AMPUAN AFZAN, KUANTAN, MALAYSIA

I declare that the copyright holders of this dissertation are jointly owned by the student and IIUM.

By signing this form, I acknowledged that I have read and understand the IIUM Intellectual Property Right and Commercialization policy.

Affirmed by Syafiq Husni Bin Mohd Murad

....

Signature Date

ACKNOWLEDGEMENT

Alhamdulillah, all praise to Allah SWT for his endless blessings that allowed myself to complete this dissertation as a compulsory requirement for the Masters of Surgery programme.

I would like to thank my hard working and dedicated supervisor, Dr Islah Munjih Bin Abdul Rashid for guiding me throughout the conduct of my thesis. His guidance and experience has much propelled me into understanding the concept of a research and completing this dissertation.

I extend my sincere gratitude to my co supervisor, Dr Hamid Hj Ghazali and the Department of Urology, the staff and OT team that made this possible and for allowing this dissertation to be conducted at Hospital Tengku Ampuan Afzan. Their help and hard work as a team proved to be vital in the success of this thesis.

Not to forget the lecturers of International Islamic University, consultants, specialist that have contributed to the study. Finally my greatest gratitude goes to my beloved wife, Dr Ami Kalsum binti Subirdan and my children – Sumayyah, Humairah, Hamzah and Luqman for all the undivided and unparalleled support. They are the pillars of my strength and whom I carve a wonderful journey that we went through these years.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

CHAPTER ONE

INTRODUCTION

1.1 BACKGROUND OF STUDY

PCNL or percutaneous nephrolithotomy is the choice of treatment for patients with large upper tract stones. PCNL is a procedure that is very effective in treating large stones, post-operatively there may have retained stone fragments that may cause significant problems in future such as recurrence and new stone formation.

There are many investigations for residual stones post PCNL such as plain kidney-ureter-bladder (KUB) radiograph, KUB ultrasonography, computerised tomography urogram (CTU), and some centres advocates routine second look nephroscopy.

Traditionally, multiple imaging studies were advocated to detect post PCNL residual stones. These imaging also were used to determine whether secondary procedures is necessary, mainly to achieve stone free status. There are many modalities to detect residual stones post PCNL. KUB radiograph remains one of the simplest modalities post PCNL imaging to detect residual stones. However, plain abdominal radiographs are less sensitive in detecting radiolucent stones and small stones, furthermore it is also insensitive as stones may be obscured by bowel gas, bony structures and obesity. This sensitivity has been demonstrated by Gettman & Pearle et al).

Michael E. Chua at al. in his study measured the Hounsfield Units of renal stones against visibility and found that the best cut-of level of HU in CT Urogram that would

predict a stone being radiolucent on KUB Radiograph is 498.5 HU. Furthermore, a Hounsfield unit of 816.51 (±274) is the cut-off point of stone to be radiolucent. Hence a HU of less than 800 would render a stone being vague radiopaque.

On the basis of this, we select patients with stones less than 800 HU whom are deemed vague radio-opaque stones undergoing PCNL and routinely perform second look nephroscopy to evaluate the incidence of retained stones and the clearance rate of PCNL for radiolucent stones.

1.2 RESEARCH QUESTIONS

i. What is the incidence of significant residual for vague-radio-opaque and radiolucent stones?

ii. What is the clearance rate of percutaneous nephrolithotomy (PCNL) for radiolucent and vague radiopaque stones?

iii. Does second look nephroscopy improve the clearance rate of vague-radio-opaque and radiolucent stones after second look nephroscopy?

1.3 OBJECTIVES

i. To determine the incidence of significant residual stones of less than 800 HU post percutaneous nephrolithotomy (PCNL)

ii. To determine the clearance rate of percutaneous nephrolithotomy (PCNL) for stones less than 800 HU

iii. To determine whether second look nephroscopy improves the clearance rate of stones less than 800 HU after second look nephroscopy

CHAPTER TWO

LITERATURE REVIEW

Complete removal of stones is the main goal in any intervention or urolithiasis to achieve a stone free status. Possible immediate adverse outcomes of stone disease and possible long term complications such as obstruction, infection, pain and future stone growth are avoided with the achievement of a complete stone removal. (Özdedeli et al).

Percutaneous nephrolithotomy (PCNL) is a very effective surgical procedure for patients with large kidney stone. The safety of the procedure have improved over the years over open stone surgery with well documented efficacy and. Stone free rates for PCNL are reported as high as 90% depending on stone properties, surgeon experience and equipment used during the procedure. (Knudsen, B. E. (2009)

Inability to access the calyces containing stone fragments, limited visualization due to bleeding, technical problems and stone composition are the main reasons for failure of complete stone clearance. Occasionally, residual fragments are left behind post operatively and a secondary procedure may be warranted.

The definition of residual stone fragments is stones fragments remaining in the urinary system after the completion of a procedure (i.e. PCNL, ESWL or URS). From literatures, clinically insignificant residual fragments (CIRFs) is defined as non-infectious, asymptomatic, and non-obstructive stone fragments which measures less than 4 mm. Of which, these fragments may occur in 70% of patients with large stones (Özdedeli et al).

Should there be no early treatment half of the patients with CRIFs will experience complications or stone related events, and among these, 50% will eventually need a secondary intervention. This is because when there is a residual stone, even CIRFs, it becomes a nidus for recurrent stone formation which later on progress to become infective, obstructive and harbour bacteria that becomes source of persistent urinary infection.

In tradition, KUB radiograph or USG KUB is used to determine any residual stones. KUB radiograph has remained a part of protocol for most clinicians even after a CT because of its impact in clinical decision making prior to treatment. Knowing the location and radio-opacity will enable the urologist to quickly decide on what treatment modality.

However, there is low sensitivity and specificity of these examinations in detecting small residual fragments. Plain radiograph will also pose a challenge in determining residual fragments should the stones are radiolucent. Radiolucency of stones on radiograph can be determined by Hounsfield Units which are numbers in standardised and convenient form obtained from a linear transformation of the attenuation from a computed tomography (CT) scan. In the case of stones, the less value of HU, the likely radiolucent the stones will appear on plain radiograph.

Michael et al demonstrated that a HU below 498.5 is identified the likeliness of a calculi to be radiolucent with a sensitivity of 89.3% and specificity of 87.3% respectively. The mean value of CT Urogram Hounsfield unit for radiolucent stones is 358.25 HU with a standard deviation of ±156, and for radio-opaque stones is 816.51 (±274). Renal stones of this value may not be visible on plain radiograph and may not

be able to determine the clearance or any residual post operatively. (Chua, M. E et al. 2012)

Multiple modalities were used to detect residual stones post PCNL. A review done by Denstead et al noted that compared to radiographic imaging, direct endoscopic inspection has greater superiority. The sensitivity of a plain abdominal film (KUB) to detect residual stones is only 34% while other imaging such as nephrotograms has sensitivity of 52% and flexible nephroscopy has sensitivity of 69%. CT Urogram have a detection rate of 47% (Sacks et al, Jewette et al 1990, 1992).

Second-look nephroscopy is a surgical procedure which the collecting system is entered percutaneously through the previously established tract in a patient who recently underwent PCNL. Intervention such as basket retrieval, endoscopic laser or basket can be used to clear remaining residual stones. (Knudsen, B. E. 2009)

Another study by Pearl et al compared sensitivity of plain radiograph, CT and flexible nephroscopy noted that, flexible nephroscopy is able to achieve overall stone free rate of 92.6%. On average, plain radiograph, CTU and flexible nephroscopy detects 0.7, 3.4 and 2.3 stones per renal unit. Sensitivity and specificity for plain radiographs are 46% and 82% and CTU has sensitivity and specificity of 100% and 62%. (Gettman, M. T., & Pearle, M. S. 2000).

Computed tomography (CT) is the gold standard in the diagnosis of urolithiasis. It provides several advantages over the kidney, urinary bladder (KUB) radiograph, such as the detection of radiolucent calculi, and sensitivity for small stones, it does not offer intervention as compared to flexible nephroscopy and not cost effective to be done on all patients post PCNL. Plus, patients are exposed to unnecessary radiation.

As detection rate may differ as stones according to radiolucency in plain KUB radiograph, while CT is not costs effective and flexible nephroscopy or second look nephroscopy has the highest detection rate, we advocate that second look may have the advantage of detecting residual radiolucent stones post PCNL.

CHAPTER THREE

METHODOLOGY

3.1 STUDY DESIGN

This is a single centre randomised control trial comparing two arms

- "PCNL only"
- "PCNL with second look nephroscopy

3.2 STUDY PERIOD

August 2015 – December 2017

3.3 LOCATION OF STUDY

Hospital Tengku Ampuan Afzan, Kuantan, Malaysia.

3.4 PATIENT RECRUITMENT

Patients are recruited from clinics and wards. The Hounsfield units of renal stones for all patients undergoing PCNL are identified through the CT Urogram via the Osirix program guided by the radiologist in the Imaging and Diagnostic Department of Hospital Tengku Ampuan Afzan.

3.5 INCLUSION CRITERIA

- All patients undergoing PCNL with pre-operative CTU of stone less than 800 HU
- Stones which are totally radiolucent on KUB radiograph but seen on CT Urogram.

3.6 EXCLUSION CRITERIA

- Patients contraindicated for PCNL
- Radio-opaque stones on plain radiograph
- Horse shoe kidney
- Pelvic kidney
- Extra-renal stones
-

3.7 STUDY HYPOTHESIS

- Routine second look nephroscopy improve the clearance rate of stones less than 800 HU.
-

3.8 NULL HYPOTHESIS

- There is no difference in clearance rate of radiolucent and vague radiopaque stones after routine second look nephroscopy.

3.9 STUDY CONDUCT

- Screened patients are identified by the principal investigator and reviewed during preoperative assessment in wards.

- Hounsfield units of the stones are determined by radiologist using Osirix DICOM viewer. Hounsfield units at three pin point area of the stones are determined and the average are taken.
- Once selection HU is obtained, other selection criteria is determined and an informed consent is obtained if patient agrees to participate.

- Agreeable patients who meet the inclusion criteria are randomised by using envelopes into two groups which are control group - PCNL Only; and intervention group – PCNL with Second Look.

- Patients in either groups will undergo PCNL with a post-operative nephrostomy tube placed.

- Post-operative plain KUB radiograph is done for both groups

- On the PCNL Only group, nephrostomy tube will be removed at day 3 post operatively if there is no complications

- On the Second Look group, patients will undergo second look nephroscopy at least after day 3 post operatively whereby any residuals will be documented and

further removal is done should there be any. Nephrostomy tube is removed post procedure.

- Post operatively, all patients will undergo KUB Ultrasound imaging at 3 months post-operatively to determine the presence of residual stones whereby a CTU would be done for further evaluation if there is presence of stones.

- Patients' records are kept in the hospital and can only be assessed by the health personnel and investigators. Results are given to the subjects and it will be extrapolated in a manner not representable to the privacy of the patient should the results be publish in any way.

- Medical records are kept for at least 5 years after patient is discharged.

3.10 SAMPLE SIZE CALCULATION

To achieve 80% statistical power and confidence level of 95% with 0.2 alpha error and 0.05 beta error, the sample size was calculated using the following formula:

$$N = [P1 (100-P1) + P2 (100-P2)] / (P2-P1)^2 \times C$$

Considering α 0.2, β 0.05, C= 7.9.

So,

$$N = [P1 (100-P1) + P2 (100-P2)] / (P2-P1)^2 \times 7.9$$

P1 =70% (clearance rate of PCNL according to previous studies)

P2 = 96% (clearance rate of PCNL with second look nephroscopy according to previous studies)

So,

$N= [70(100-70) + 96(100-96)] / (96-70)^2 \times 7.9$

$= [70(30) + 96(4)]/26^2 \times 7.9$

$= [2100+384]/676 \times 7.9$

$= [2484/676] \times 7.9$

$=29.02899$

=30 patients in each study arm

Considering a dropout rate of 10% = 3 patients

Final n = **33 patients in each study arm**

3.11 STATISTICAL ANALYSIS

Statistical analysis of my study will be conducted using IBM SPSS Statistics version 20. Descriptive statistics will be presented as frequency and percentage for categorical data. Numerical data will be presented as mean and standard deviation in normally distributed data and median and IQR in not normally distributed data. A P-value < 0.05 is considered statistically significant. Analysis will be done using Chi Square along with Fisher exact test.

CHAPTER FOUR

RESULTS AND FINDINGS

4.1 PATIENT / SAMPLE RECRUITMENT

A total of 69 patients were recruited in this study. Nine patients were dropped out from this study, by which 5 patients defaulted follow up ultrasound KUB and 4 patient refused to be consented in the study. Sixty patients were eligible to be participated in this study and equally randomized to 30 samples in each arms designated as “PCNL Only” and “PCNL with Second Look Nephroscopy”

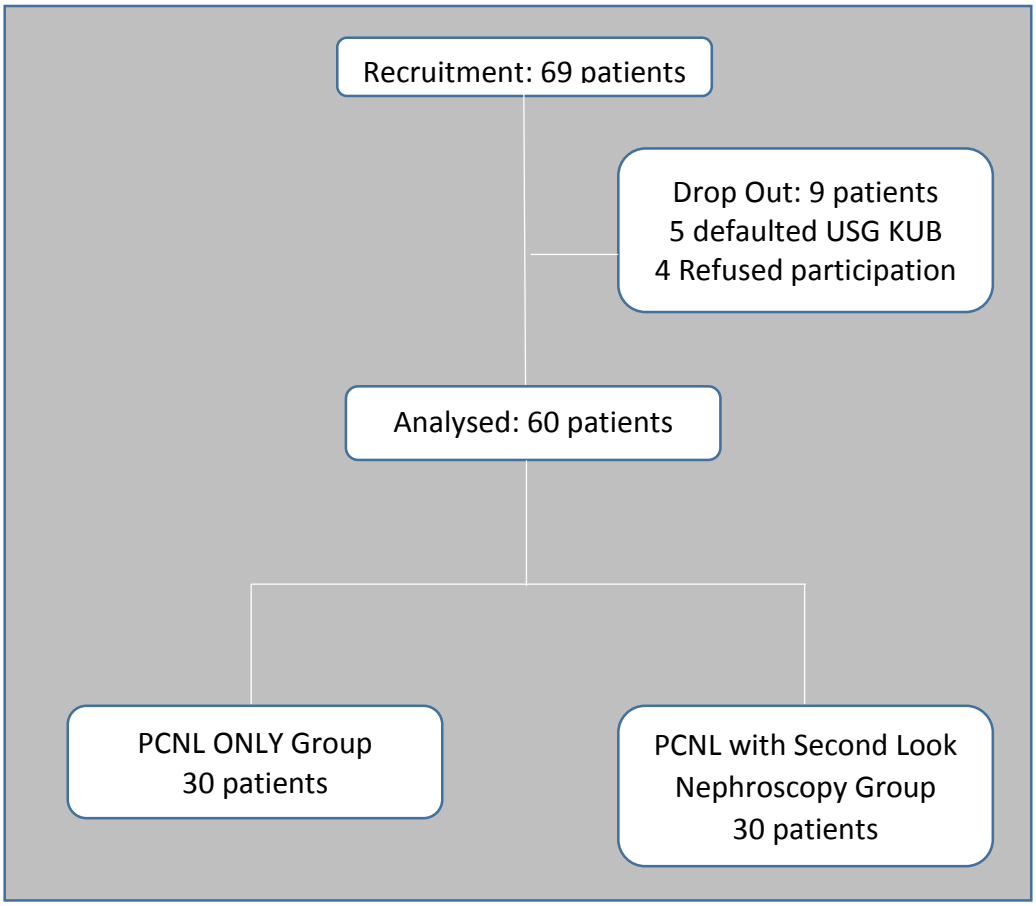

Figure 4.1 Sample and Recruitment Process

4.2 DEMOGRAPHICS AND CLINICAL DATA

The median age for all patients were 55 with a range of 18-70 years old. Overall median age between the PCNL Only and PCNL + Second Look were 50 and 58 respectively with a range of 18-70 and 26-66 respectively.

Overall, the distribution of the male and female across both groups were homogenous with p value of 0.305. The BMI distribution fares slightly higher in the PCNL + Second Look group however it is still not significantly different with a p value of 0.36. The Hounsfield units for all the patients in this study has a median of 472 HU with a range of 215-768 HU. The median value of both arms are 479.5 HU and 465 HU respectively with overall distribution is homogenous.

Patients in the intervention group has a longer duration of stay of average of 1 day compared to the PCNL Only group however generally patients have a range stay of 3-6 days.

Table 4.1 Baseline Demographics Characteristics of all patients, PCNL only and PCNL with second look nephroscopy.

Characteristics	**All Patients (n = 60)**	**PCNL Only (n = 30)**	**PCNL + Second Look (n = 30)**	**P Value**
Age, y, range	55 (18-70)	50 (18-70)	58 (26-66)	0.517
Male, n, %	38 (63.3)	20 (66)	18 (60%)	0.305
Female, n, %	22 (36.7)	10 (33)	12 (40%)	0.305
BMI, kg/m^2, median, (range)	25.8 (16.9-45.7)	24.8 (16-39)	28.8 (19-45)	0.036
Hounsfield Unit, Hu, median, (range)	472 (215-768)	479.5 (275-739)	465 (215-768)	0.794
Duration of Stay, days, median (range)	4 (3-6)	3 (3-5)	4 (3-6)	0.880

4.3 PREOPERATIVE CHARACTERISTICS OF ALL PATIENTS AND BOTH ARMS

Preoperatively, visibility of stones from KUB X-Ray for all the patients in the study is 41.7%. Fifteen patients (50%) in the PCNL Only group and 10 (33.3%) patients in the PCNL + Second Look has visible stones on KUB X-Ray.

Otherwise stone size between the two groups are homogenous with median stone size of 2.2 and 2.4 on the control and intervention group respectively with a p value of 0.053. The location of stones are significantly more in the pelvic-ureteric junction in the PCNL Only arm compared to the PCNL + Second Look arm, otherwise it is homogenously distributed across both groups.

Table 4.2 Preoperative Demographics Characteristics of all patients, PCNL only and PCNL with second look nephroscopy in terms of visibility and stone size.

Characteristics	**All Patients (n = 60)**	**PCNL Only (n = 30)**	**PCNL + Second Look (n = 30)**	**P Value**
Visibility on KUB-XR, n, (%)	25 (41.7)	15 (50)	10 (33)	0.062
Stone size, cm, median, (range)	2.2 (1.0-5.4)	2.2 (1.2-3.5)	2.4 (1.0-5.4)	0.053