

**A RETROSPECTIVE STUDY ON
PREDICTIVE RISK OF
INFECTION COMPLICATION
POST PERCUTANEOUS NEPHROLITHOTOMY
IN HOSPITAL UNIVERSITI SAINS MALAYSIA
FROM 2013 TO 2018**

DR RAZIF BIN ISMAIL

**DISSERTATION SUBMITTED IN PARTIAL
FULFILLMENT OF THE REQUIREMENTS FOR THE
DEGREE OF MASTER OF GENERAL SURGERY**



USM UNIVERSITI
SAINS
MALAYSIA



UNIVERSITI SAINS MALAYSIA

2021

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ACKNOWLEDGEMENTS

Bismillahirrahmanirrahim.

All praise and thanks to Allah the Almighty who consistently guides me to the right path and providing strength for me to complete the journey as a postgraduate student.

Firstly, I would like to thank my dissertation supervisors, Associate Professor Dr Andee Dzulkarnaen Zakaria (Colorectal Surgeon and Senior Lecturer of Department of Surgery, Hospital Universiti Sains Malaysia) and my co-supervisor, Dr Mohamed Ashraf Mohamed Daud (Urologist and Lecturer of Department of Surgery) for their support and guidance throughout my dissertation journey that has been an tense process for its completion.

My greatest gratitude to my parents and family in Tamparuli, Sabah and my foster family in Segamat, Johore for their continuous support in motivating and aspiring me throughout my entire life. So, goes to my colleagues (doctors, statistician and record office staffs) in giving a hand especially during data collection and data analysis.

Hopefully, this dissertation would be a steppingstone towards a better and fruitful ride for me as a general surgeon in the future. Thank you very much, may Allah reward you with Jannah in life hereafter.

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LIST OF SYMBOLS, ABBREVIATIONS AND ACRONYMS

ACCP	American College of Chest Physician
Adj. OR	Adjusted Odd Ratio
AUA	American Urology Association
CI	Confidence Interval
CROES	Clinical Research of the Endourological Society
CT	Computed Tomography
EAU	European Association of Urology
<i>E. coli</i>	<i>Escherichia coli</i>
FBS	Fasting Blood Sugar
HAI	Hospital Acquired Infection
HUSM	Hospital Universiti Sains Malaysia
IVU	Intravenous Urography
IQR	Interquartile Range
KUB	Kidney, Ureter and Bladder
LR	Logistic Regression
OR	Odd Ratio
PaCO ₂	Partial Pressure of Arterial Carbon dioxide
PCNL	Percutaneous Nephrolithotomy
RBS	Random Blood Sugar
RPP	Renal Pelvis Pressure
SCCM	Society of Critical Care Medicine
SD	Standard Deviation
SIRS	Systemic Inflammatory Response Syndrome

SPSS	Statistical Package for Social Science
UTI	Urinary Tract Infection
USM	Universiti Sains Malaysia
X^2	Chi-Square Test

**Kajian Retrospektif Tentang Ramalan Risiko Jangkitan Selepas Pembedahan
Batu Karang Buah Pinggang Menggunakan Skop Menerusi Kulit Ke Dalam Buah
Pinggang Di Hospital Universiti Sains Malaysia Daripada
Tahun 2013 Hingga 2018**

ABSTRAK

Pengenalan: Pembedahan batu karang buah pinggang menggunakan skop menerusi kulit ke dalam buah pinggang (PCNL) adalah prosedur standard untuk batu karang buah pinggang yang besar dan kompleks semenjak ianya diperkenalkan sebagai prosedur endourologi semenjak 4 dekad lepas. Walaupun prosedur ini selamat, terdapat komplikasi yang boleh berlaku dan ianya telah dilaporkan dalam penulisan terdahulu. Kajian ini bertujuan untuk menyiasat faktor-faktor sebelum dan semasa pembedahan dijalankan yang menjadi peramal kepada komplikasi jangkitan selepas pembedahan di Hospital Universiti Sains Malaysia.

Kaedah: Kajian ini adalah kajian retrospektif yang melibatkan pesakit yang menjalani pembedahan PCNL daripada tahun 2013 hingga 2018 di sebuah institusi penyelidikan di hospital yang berada di Pantai Timur Malaysia. Pembolehubah dikategorikan kepada faktor-faktor risiko sebelum dan semasa pembedahan serta hubungannya dengan terjadinya demam, sindrom tindak balas radang sistemik (SIRS) dan sepsis selepas pembedahan. Pelbagai analisis regresi logistik digunakan untuk menentukan faktor yang berkaitan dengan terjadinya jangkitan. Data dianalisis dengan menggunakan perisian SPSS versi 26.

Keputusan: Seramai 86 orang pesakit dikenapasti telah menjalani pembedahan PCNL yang memenuhi kriteria inklusi kajian. Kadar prevalens komplikasi jangkitan adalah

sebanyak 31.4% (95% CI=21.8,42.3), SIRS sebanyak 17 pesakit (n=19.8%) dan sepsis sebanyak 6 pesakit (n=7%). Kajian ini mendapati bahawa tiada kaitan yang signifikan antara umur, komorbiditi, kumpulan etnik, durasi pembedahan dan pembengkakan pelvis buah pinggang kepada berlakunya komplikasi jangkitan. Pesakit yang mendapat jangkitan berhubungkait dengan pemilihan antibiotik profilaksis ($p=0.036$), positif kuman air kencing sebelum pembedahan ($p<0.001$), adanya tiub buah pinggang ke kulit dan tiub ureter ($p=0.004$), albumin yang rendah ($p=0.043$), memerlukan transfusi darah ($p=0.001$), berbaki batu karang selepas pembedahan ($p=0.008$), jumlah batu karang yang besar ($p=0.001$) dan lebih lama menetap di hospital ($p<0.001$). Menerusi pelbagai analisis regresi logistik, pemilihan antibiotik berbanding dengan kumpulan cephalosporin (Nisbah odds yang diperbetulkan=17.77, 95% sela keyakinan: 2.38, 209.91; $p=0.009$), adanya tiub buah pinggang dan tiub ureter (Nisbah odds yang diperbetulkan=7.14, 95% sela keyakinan:2.39,209.91; $p = 0.021$) dan lebih lama menetap di hospital (Nisbah odds yang diperbetulkan=1.85, 95% sela keyakinan: 1.30, 2.95; $p = 0.003$) adalah faktor risiko bebas yang mempunyai hubungan dengan peningkatan komplikasi jangkitan selepas PCNL.

Kesimpulan: Risiko untuk terjadinya sepsis selepas PCNL adalah rendah. Pemilihan jenis antibiotik, adanya tiub buah pinggang and tiub ureter serta lebih lama durasi menetap di hospital adalah faktor-faktor yang mempunyai hubungan dengan terjadinya komplikasi jangkitan. Oleh itu, sekiranya pesakit mempunyai risiko tersebut, pakar urologi hendaklah lebih berwaspada dan pesakit seharusnya dinasihati lebih awal tentang komplikasi jangkitan terutamanya terjadinya sepsis.

Kata kunci: batu karang buah pinggang, pembedahan PCNL, SIRS, sepsis, batu karang staghorn

**A retrospective study on predictive risk of infection complication post
percutaneous nephrolithotomy in Hospital Universiti Sains Malaysia from
2013 to 2018.**

ABSTRACT

Background: Percutaneous nephrolithotomy (PCNL) has become a standard procedure in a large, complex stone of the upper urinary tract since it was introduced into the endourologist's armamentarium 4 decades back. Though the procedure is safe, complication still occur and are well reported in literature. This study aims to investigate the pre- and intraoperative predictors on infective complication in patient undergoing PCNL in Hospital Universiti Sains Malaysia.

Methodology: This is a retrospective cohort study in a single institution involving patients undergoing PCNL between 2013 and 2018 in a teaching hospital at East Coast Malaysia. The variables were categorized into preoperative risk factors and intraoperative risk factors and the outcomes measured include infection complications of fever, systemic inflammatory response syndrome (SIRS) and sepsis. Multiple logistic regression analysis was used to determine independent risk factor associated with infective complication. Data were analysed using SPSS version 26.

Result: We identified 86 consecutive patients who underwent primary PCNL that fulfil the inclusion criteria. The prevalence of infective complications was 31.4% (95% CI = 21.8,42.3), SIRS 17 patients (n=19.8%) and sepsis 6 patients (n=7%). There was no significant association between age, present of comorbidities, ethnicity, present of hydronephrosis and duration of surgery with the occurrence of infective complications. Those with infective complications were more likely to be associated with choice of

prophylaxis antibiotics ($p=0.036$), positive pre-operative urine culture ($p < 0.001$), presence of nephrostomy tube or ureteric stent ($p=0.004$), lower albumin level ($p=0.043$), positive perioperative blood transfusion ($p=0.001$) presence of residual stone post-PCNL ($p=0.008$), heavier stone burden ($p=0.001$) and longer hospital stay ($p<0.001$). In multivariable analysis, the choice of other antibiotic in comparison with cephalosporin group (Adj. OR 17.77, 95% CI:2.38,209.91; $p=0.009$), presence of nephrostomy tube or ureteric stent (Adj. OR 7.14, 95% CI:2.39,209.91; $p=0.021$) and longer duration of hospital stay (Adj. OR 1.85, 95% CI:1.30,2.95; $p=0.003$) are independently associated with increased risks of infective complication post PCNL.

Conclusion: The risk of individuals undergoing PCNL to developed sepsis is low. The choice of prophylaxis antibiotics, presence of nephrostomy tube or ureteric stent and length of stay were found as independent risk factors to develop infective complications. Thus, the presence of these risk factors should be alert the treating urologists and patients regarding the risk of detrimental complications especially sepsis.

Keywords: nephrolithiasis, percutaneous nephrolithotomy, systemic inflammatory response syndrome, sepsis, staghorn calculi

CHAPTER 1

INTRODUCTION

1.1 Literature Review

Percutaneous nephrolithotomy (PCNL) is a minimally invasive procedure designed to remove complex stone or large stone inside the upper urinary tract namely the renal calyces, renal pelvis and upper ureter. According to the American Urology Association (AUA), PCNL is recommended as the first-line treatment for stone size more than 2cm, multiple stones and inferior calyx renal stone (1). Since the initial description by Fernstrom and Johansson in 1976 whose technique involved the extraction of renal stone via the nephrostomy tube under radiological control, the procedure has emerged as the gold standard treatment for large and complex stones at the upper urinary tract (2). The procedure has evolved with numerous innovations in terms of instruments, improvement of the renal access and techniques which remarkably yield high stone-free rates with low complication rate (3).

In general, PCNL is a safe procedure as it is less invasive compare to other alternatives such open nephrolithotomy and open pyelolithotomy in the past with comparable stone clearance rate. However, various complications are associated with the procedure such as bleeding, infection, pneumothorax, haemothorax, urine leakage from the nephrocutaneous fistula and rupture of the pelvicalyceal system (4). In several series assessing the outcomes of the procedure, sepsis was reported as the most common cause of perioperative mortality. An example of a large series which report the incidence of sepsis causing mortality post PCNL is O' Keefe et al in 1993, reported six incidences of mortality secondary to sepsis among 700 patients undergoing PCNL (5). Another series,

the Clinical Research of the Endourological Society (CROES) study has identified two incidences of mortality due to sepsis among international cohort of more than 5,000 patients. A less severe infectious complications post PCNL are more frequent in comparison to the incidence of sepsis. In CROES study, 598 patients (10.5%) developed post-operative fever, while urinary tract infection with proven positive urine culture for organism developed in 30 patients (0.6%) and sepsis developed in fewer than 10 patients (0.2%) (6). Thus, it is important for the treating surgeons to identify the factors that may contribute to development of sepsis and appropriate actions need to be implemented to avoid morbidity and mortality.

1.2 Study Rationale

To date, no published Malaysian data regarding the number of patients undergoing PCNL and the overall outcomes of the procedure including its effectiveness in achieving free-stone rates and perioperative complication. However, the readily available international series had identified several risk factors associated with development of infection and sepsis complications post PCNL. Despite the available data, the independent risk factor associated with infection complication postoperatively was inconsistent. Thus, the authors embark on this study to identify the prevalence of infection complication post PCNL and the risk factors of infection complication among patients undergoing PCNL in Hospital Universiti Sains Malaysia (HUSM). The early recognition of the risks may increase the patients and clinician's awareness regarding the possible complication and thus early intervention is carried out to improve patient's overall outcomes.

CHAPTER 2
STUDY PROTOCOL

Study protocol submitted for ethical approval.

RESEARCH PROPOSAL FOR MASTER OF MEDICINE
PARTIAL REQUIREMENT FOR MASTER OF MEDICINE (GENERAL
SURGERY) PROGRAMME UNIVERSITI SAINS MALAYSIA

Research title:

A Retrospective Study on Predictive Risk of
Infection Complication Post Percutaneous Nephrolithotomy
in Hospital Universiti Sains Malaysia
from 2013 to 2018

Protocol number:

USM/JEPeM/19070420

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2.1 Introduction

Percutaneous nephrolithotomy (PCNL) is a minimally invasive procedure, specifically designed to remove complex stone or large stone inside the upper urinary tract namely the renal calyces, renal pelvis and upper ureter. The PCNL is recommended as the first-line treatment for stone size more than 2cm, multiple and inferior calyx renal stone according to the American Urology Association (AUA) (Preminger, Assimos et al. 2005). Since the initial description in 1976 by Fernstrom and Johansson whose technique involved the extraction of renal stone via the nephrostomy tube under radiological control, the procedure has emerged as the gold standard treatment for large and complex stone at the upper urinary tract (Fernström and Johansson 1976). The techniques have evolved with numerous innovations in terms of instrument used, nephroscope replaced the rigid cystoscope in 1980s and radiographic innovation including the improvement of fluoroscopy to ease the renal calyceal access. Apart from that, the development of various lithotripsy devices and the introduction of the holmium laser aid in fragmentation of large stone. The advent of modern PCNL with improvement of the renal access, technique, instrument and experience would yield high stone-free rates and might reduce the complication rate (Patel and Nakada 2015).

In general, PCNL is considered as a safe procedure considering its high stone-free rates and less morbidity compared to another alternative modality such as open nephrolithotomy or open pyelolithotomy in the past. However, serious complication may happen and should be suspected following the procedure. Complications such as perioperative bleeding, infectious complication including fever and sepsis, thoracic complication such as pneumothorax and haemothorax, urine leakage from the nephrocutaneous fistula, rupture of the pelvicalyceal system and adjacent organ injury are

well documented by many authors (Kyriazis, Panagopoulos et al. 2015). Of these, post-operative fever is the commonest and are mostly secondary to UTI. In more serious complications related to infective complication, pyelonephritis and sepsis need to be aware as these might need to be treated with longer duration of antibiotics and subsequently prolonged patient's hospital stay.

In several series assessing the outcomes of the procedure, sepsis was reported as the most common cause of perioperative death. Thus, it is important for the treating surgeons to identify the factors that may contribute to development of sepsis and appropriate actions need to be implemented to avoid morbidity and mortality. An example of large series which report the incidence of sepsis causing mortality post PCNL is O'Keefe et al in 1993, reported six incidence of mortality secondary to sepsis among 700 patients underwent PCNL (O'keeffe, Mortimer et al. 1993). Another series, the Clinical Research of the Endourological Society (CROES) study has identified two incidences of mortality due to sepsis among international cohort of more than 5,000 patients. A less severe infectious complications post PCNL are more frequent in comparison to the incidence of sepsis. In CROES study, 598 patients (10.5%) developed post-operative fever, while urinary tract infection with proven positive urine culture for organism developed in 30 patients (0.6%) and sepsis developed in fewer than 10 patients (0.2%) (Labate, Modi et al. 2011).

To date, there is no published Malaysian data regarding the number of patients undergoing PCNL and the overall outcomes of the procedure including its effectiveness in achieving free-stone rates and perioperative complication. However, the readily available international series had identified several risk factors associated with development of infection and sepsis complications post PCNL. Thus, this study is

designed mainly to identify the prevalence of infection complication post PCNL and the risk factors of infectious complication among patients underwent PCNL in Hospital Universiti Sains Malaysia (HUSM). The early recognition of the risks may increase the patient and clinician awareness regarding the possible complication and thus early intervention is carried out to improve patient's overall outcomes.

2.2 Problem Statement and Study Rationale

According to the AUA, percutaneous nephrolithotomy is the first-line treatment recommendation for a stone size >2cm, multiple and inferior calyx renal stone. In a study of the prevalence of kidney stone disease among patients admitted to HUSM in 5 years, since 1st January 2012 to 21st December 2016. Among 86,039 patients admission age 18 years old and above, the prevalence of nephrolithiasis as the reason of admission was 1.8% and among these patient, 10.3% of patients suffered from staghorn calculi (Nouri and Hassali 2018). This indicates that the disease itself is considered as common among the population live in Kelantan. The availability of urology service in HUSM ensured proper treatment is given to patient according to the guideline and the standard procedure is performed by qualified personal.

There are many health centres in Malaysia including private hospitals offering urology services and PCNL. However, the researcher found that there is lacking in publication of Malaysian data with regard to studies involving percutaneous nephrolithotomy. As mentioned earlier, this study is designed to determine the prevalence and to identify the risk factors of infective complication among patients undergoing PCNL in HUSM. The result of this study may be significant yet comparable with the

international studies. The understanding and recognition of the preoperative risks as well as intraoperative risks of infectious complication post PCNL may increase the awareness of the treating team and thus early intervention can be done to improve patient's overall outcomes.

In general, the predictive risks of infection complication can be divided broadly into preoperative risks and intraoperative risks. Various authors presented their studies to find out the risk factors for infectious complications after PCNL. The significant preoperative risk factors include patient's demographics (age, gender and comorbid), positive urine culture, severity of hydronephrosis, size of stone and presence of nephrostomy tube. While the intraoperative risk factors include blood transfusion and length of operation. With these known risk factors for post-operative infection complication post PCNL, there can be compared with the results obtained from this study.

2.3 Benefit of the study

1. Institution:

1.1. To determine how often PCNL is done in HUSM.

1.2. Able to determine the prevalence of infective complications post PCNL in HUSM.

1.3. As a reference for further study with a better design in urology centers in Malaysia.

1.4. Able to compare the risk factors of infection complication post PCNL with other institution.

1.5. For a better operative planning and reduce the hospital financial burden by proper identification of high-risk patients.

2. Healthcare worker:

2.1. Increase awareness among the treating surgeon or treating team to initiate early intervention following the procedure to avoid severe complication.

3. Patient:

3.1. This may help to screen patients at risk of developing post-operative infection complication, thus precaution done to reduce patient's morbidity.

2.4 Research Questions

1. What is the prevalence of infective complications among patients undergoing percutaneous nephrolithotomy in HUSM?
2. What are the preoperative risk factors associated with infective complications post PCNL in HUSM?
3. Is there intraoperative risk factor associated with infective complications post PCNL in HUSM?

2.5 Objectives

2.5.1 General objective

To determine the prevalence of infective complications post PCNL in HUSM.

2.5.2 Specific objectives

- 1) To determine the preoperative risk factors for infective complications post PCNL in HUSM.
- 2) To determine the intraoperative risk factors for infective complications post PCNL in HUSM.

2.6 Research Hypothesis:

H₀: There is no association between risk factors (gender, diabetes mellitus, stone size, positive preoperative urine culture, present of hydronephrosis, preoperative nephrostomy tube insertion, prolonged duration of operation and intraoperative blood transfusion) and infective complication post PCNL.

H₁: There is association between risk factors (gender, diabetes mellitus, stone size, positive preoperative urine culture, present of hydronephrosis, preoperative nephrostomy tube insertion, prolonged duration of operation and intraoperative blood transfusion) and infective complication post PCNL.

2.7 Literature Review

Sreenevasan G. presented the incidence of urinary calculi in the kidney plus ureter and other parts of the urinary tract in 1980 and 1989 among Malaysian population. The author conducted the studies in 1980 that covered the year 1962 to 1976 and another study conducted in 1989 that covered the year 1977-1981. The data was analysed in per 100,000 populations and it shows steady increase in the incidence of nephrolithiasis and other type of urolithiasis. It also studied the incidence of urolithiasis among major ethnicities in Malaysia (Malay, Chinese and Indian), sex and age distribution. Of more than four thousand patients recruited, 48% were Chinese, 37% were Malay and 13% were Indian. The incidence of nephrolithiasis based on age distribution is highest between 30-50 years old in all ethnics and domination in male compare to female (Sreenevasan 1990).

A more recent data by Nouri and Hassali in 2018 presented the prevalence of kidney stone disease among patients admitted to University Science Malaysia Hospital (HUSM) from 1st January 2012 to 21st December 2016. A total number of admissions to this hospital were 199,318 while of these numbers, 86,039 patients age 18 years above. The prevalence of nephrolithiasis was 1.8% of total admission with male to female ratio of 1.35:1. A total of 56.8% patients had single stone while another 43.25% had multiple stones. Of these, 10.3% of patients suffered from staghorn calculi (Nouri and Hassali 2018).

PCNL is the gold standard treatment among patients with large and complex stone which yield stone-free rates achieving more than 90% (Skolarikos, Alivizatos et al. 2005). The diagnosis of renal stone was made by plain X-ray kidney, ureter and bladder (KUB) and confirmed with either intravenous urography (IVU) or computed tomography (CT)

urography or CT KUB for radiolucent stones. The renal stones that occupied the renal pelvis and two or more calyces were defined as staghorn calculi.

A standard PCNL procedure was done in all patients. The procedure was done under general anaesthesia, a retrograde ureteric catheter was placed and fixed to Foley's catheter in which it was used to fill-up contrast fluid. The patient was positioned to prone and the initial puncture with 18-gauge needle done. The tract was dilated with Alkens dilator and a 24 or 26 Fr Amplatz sheath was placed. A 22 Fr rigid nephroscope was placed and various techniques for fragmentation and removal of the stone done. A nephrostomy tube was placed before the end of the procedure (Bansal, Pawar et al. 2017).

PCNL yield a higher risk to develop infection compare to other clean contaminated surgery or other endourological procedure due to several reasons. First, due to the larger and complexity of the stone, bacterial colonization might not permit sterilization of the urine despite of antibiotics treatment preoperatively. This effect was well documented by a study conducted by Fowler and colleagues, who demonstrated the presence of pathogenic bacteria inside the extracted stone which was soaked with antibacterial solution for several hours. Apart from that, the stagnant or obstructive urinary system caused by the stone impaired the drainage of infected fluid thus creating an abscess-like bacterial niche. Lastly, the nature of minimally invasive surgery which create a small opening and required optimize field of operation tend to increase the intrarenal pressure, contributing to pyelotubular, pyelolymphatic and pyelovenous back-flow which promotes bacterial translocation into the systemic circulation. When access to renal pelvis was obtained via calyceal puncture, it disrupted the normal endothelium and thus exposed the lymphatic and venous channels to the pelvis environment and irrigation fluid (Kreydin and Eisner 2013). Zhong *et. al* presented the incidence of post-

operative fever was significantly higher ($p=0.037$) in patient with renal pelvis pressure (RPP) of >20 mmHg compare to RPP of <20 mmHg (Zhong, Zeng et al. 2008).

Postoperative infective complication has wide range of definition. This includes postoperative fever with clinical significant of more than 38°C within hospital stay, patient experienced systemic inflammatory response syndrome (SIRS) according to the American College of Chest Physicians (ACCP) and the Society of Critical Care Medicine (SCCM) in 2001 (two or more positive of the following): 1) body temperature $>38^{\circ}\text{C}$ or $<36^{\circ}\text{C}$, 2) heart rate of >90 beats per minute, 3) respiratory rate of >20 breaths per minute or partial pressure of arterial carbon dioxide (PaCO_2) <32 mmHg, 4) White cell count $>12,000$ cells/uL or $<4,000$ cells/uL. Sepsis was defined as both SIRS and evidence of infection present either positive blood culture or urine culture (Levy, Fink et al. 2003).

Both prospective and retrospective studies presented multiple risk factors associated with infectious complication post PCNL. The authors have divided them into preoperative and intraoperative risks factors which look at various infection complication including fever, SIRS and sepsis. With regards to preoperative risk factors; firstly, in term of patient's demography, a cross sectional study conducted by Sharifi Aghdas *et al.* in 2006 presented female gender has significant association with postoperative fever following PCNL (Aghdas, Akhavizadegan et al. 2006). While, Gutierrez *et al.* in 2012 with large number of patients recruited in the study presented patient with comorbid diabetes has significant association with postoperative fever. In the very similar study, it yielded positive preoperative urine culture has significant association with postoperative fever (Gutierrez, Smith et al. 2013). Apart from this study there are few more studies that have significant association for preoperative positive urine culture with fever post PCNL. Both Sharifi Aghdas *et al.* and Gutierrez *et al.* presented significant correlation between

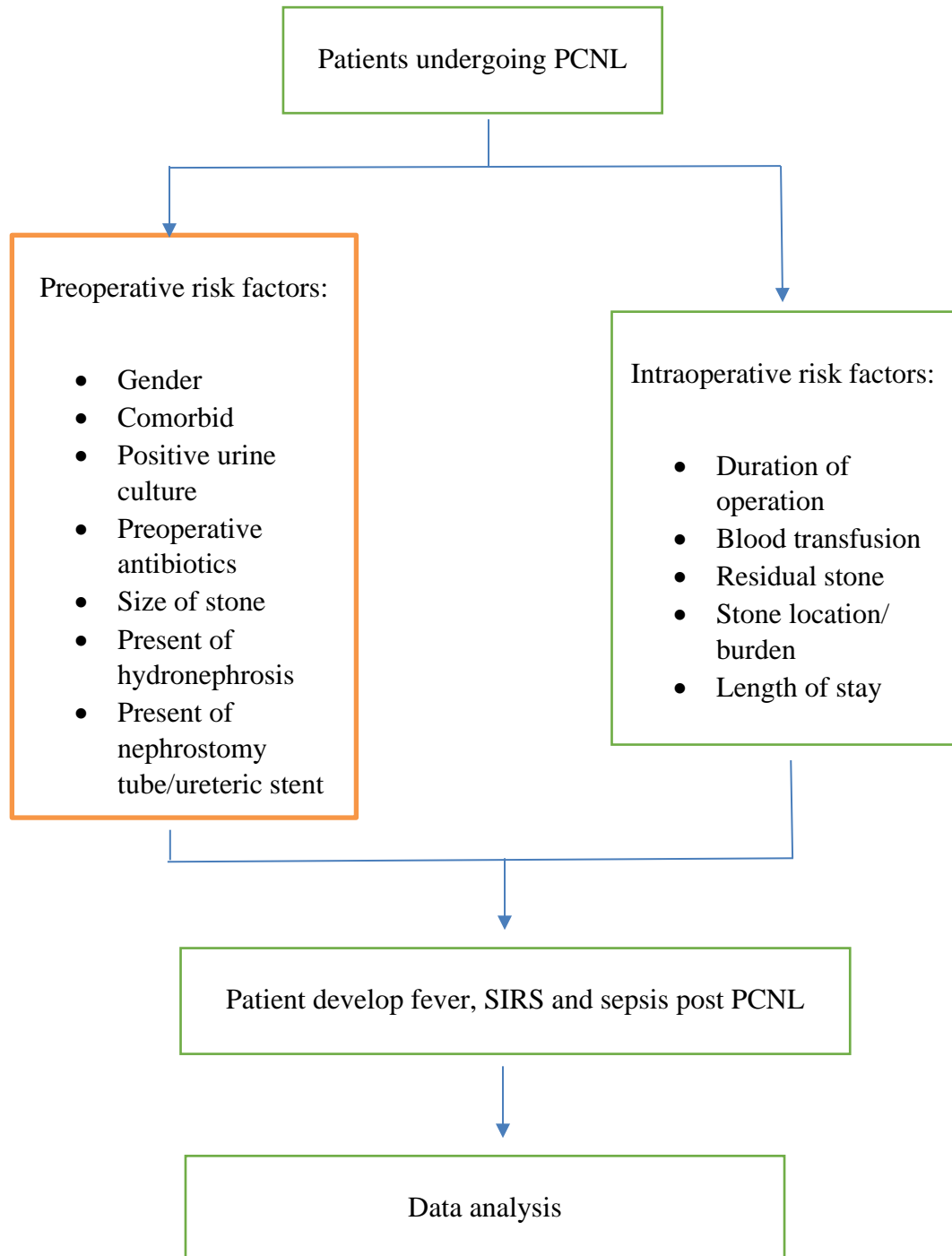
preoperative nephrostomy tube and postoperative fever post PCNL (Aghdas, Akhavizadegan et al. 2006, Gutierrez, Smith et al. 2013).

Gonen *et al.* in 2008 conducted a prospective study regarding factors affecting fever following PCNL and found out there were significantly higher incidence in patients with larger stone burden (Gonen, Turan et al. 2008). Besides, a retrospective study conducted by Bansal *et al.* in 2017 presented a significant correlation with postoperative fever post PCNL with stone size >25mm (Bansal, Pawar et al. 2017). Chen *et al.* in 2008 found out the presence of hydronephrosis has significant association with fever post PCNL (Chen, Xu et al. 2008). Besides, study conducted by Kuldeep Sharma in 2016 presented a significant association of moderate to severe hydronephrosis with infection post PCNL (Sharma, Sankhwar et al. 2016).

In comparison with preoperative risk factors, there are not much intraoperative risk factors associated with infection complication post PCNL. Most of the studies looked at the duration of operation and significant bleeding which required blood transfusion. Chen *et al.* and Gonen *et al.* indicated the longer operation time is significantly associated with fever post PCNL. While Bansal *et al.* presented significant association among patient undergoing operation >120 minutes compared to <120 minutes with fever post PCNL (Chen, Xu et al. 2008, Gonen, Turan et al. 2008, Bansal, Pawar et al. 2017). Chen *et al.* also discovered that there is significant association between blood transfusion for significant bleeding intraoperatively and occurrence of fever (Chen, Xu et al. 2008).

2.8 Conceptual Framework

Figure 2.1: Conceptual framework



2.9 Methodology

2.9.1 Research Design

This is a retrospective review of medical records in HUSM, Kubang Kerian, Kelantan from June 2013 to May 2018. The participants involved are all patients underwent percutaneous nephrolithotomy in HUSM that fulfil the inclusion and exclusion criteria.

2.9.2 Study Area

Hospital Universiti Sains Malaysia (teaching hospital), Kubang Kerian, Kelantan.

2.9.3 Study Population

Reference population: All patients who have staghorn calculi or renal stone of more than 2cm that are indicated for percutaneous nephrolithotomy in Hospital USM.

Source population: All patients underwent percutaneous nephrolithotomy in Hospital Universiti Sains Malaysia.

Study population: All patients underwent percutaneous nephrolithotomy in Hospital Universiti Sains Malaysia who fulfil the inclusion and exclusion criteria.

2.9.4 Subject Criteria

Inclusion criteria:

1. Patient's age 18 years old and above.
2. Underwent percutaneous nephrolithotomy in HUSM within the 5 years of study period (1st June 2013 to 31st May 2018).
3. No documented renal congenital abnormality.
4. Unilateral percutaneous nephrolithotomy.

Exclusion criteria:

1. Patient's with underlying congenital renal abnormality.
2. Second look percutaneous nephrolithotomy.
3. Age less than 18 years old.
4. Patient underwent bilateral percutaneous nephrolithotomy at same setting.
5. Patient with active infection prior to operation.

2.9.5 Sample Size Estimation

The estimated sample size is **86 subjects** based on calculation below:

Objective 1:

To determine the prevalence of infection complication post PCNL in HUSM, the sample size estimation will be calculated based on single proportion formula.

$$n = (Z_{\alpha/d})^2 \times P(1-P)$$

P= 11% or 0.11 proportion of patient underwent PCNL had infection complication

d= precision or detectable deviation. We take as 8% (0.08), usually take between 1% (0.01) to 10% (0.1)

Z_α= normal deviates that reflects Type I error, 1.96 for α=0.05 (level significant 5%, 95% confidence interval)

$$\text{So, } n = (1.96/0.08)^2 \times 0.11(1-0.11), n = 58$$

$$n + 20\% \text{ drop out} = 58 + 12$$

$$n = 70$$

Objective 2 and 3:

To determine the association between infection complication post PCNL with the preoperative risk factors (gender, comorbid diabetes, stone size, positive urine culture, present of hydronephrosis and nephrostomy) and intraoperative risk factors (duration of operation and blood transfusion), sample size was estimated based on the literature review and calculated using Power and Sample size (PS software).

P= 0.05

(B) Power= 80%

P₀: Proportion of patient with risk factor does not develop infection complication post PCNL

P₁: Estimated proportion of having risk factors has developed infection complication post PCNL

Power and Sample Size Program: Main Window

File Edit Log Help

Survival t-test Regression 1 Regression 2 Dichotomous Mantel-Haenszel Log

Output

[Studies that are analyzed by chi-square or Fisher's exact test](#)

[What do you want to know?](#) Sample size

[Case sample size for uncorrected chi-squared test](#) 35

Design

[Matched or Independent?](#) Independent

[Case control?](#) Case-Control

[How is the alternative hypothesis expressed?](#) Two proportions

[Uncorrected chi-square or Fisher's exact test?](#) Uncorrected chi-square test

Input

α 0.05 p_0 0.32

$power$ 0.8 p_1 0.65

m 1

Calculate

Graphs

Description

We are planning a study of independent cases and controls with 1 control(s) per case. Prior data indicate that the probability of exposure among controls is 0.32. If the true probability of exposure among cases is 0.65, we will need to study 35 case patients and 35 control patients to be able to reject the null hypothesis that the exposure rates for case and controls are equal with probability (power) 0.8. The Type I error probability associated with this test of this null hypothesis is 0.05. We will use an uncorrected chi-squared statistic to evaluate this null hypothesis.

Table 2.1: Objective 2 and 3 sample size calculation

Associated factor/ outcome	P	Power	❖ P₀	P₁ (Estimation)	n	Total n (n + 20%) x2	❖ Study
Female gender with infection complication	0.05	0.8	0.32	0.65	33	84	(Rivera, Viers et al. 2016)
Diabetes with infection complication	0.05	0.8	0.1	0.4	32	76	(Rivera, Viers et al. 2016)
Stone size >25mm with infection complication	0.05	0.8	0.42	0.75	34	82	(Bansal, Pawar et al. 2017)
Positive urine culture with infection complication	0.05	0.8	0.25	0.6	30	72	(Rivera, Viers et al. 2016)
Hydronephrosis with infection complication	0.05	0.8	0.53	0.2	32	76	(Yang, Liu et al. 2017)
Nephrostomy with infection complication	0.05	0.8	0.51	0.2	36	86	(Aghdas, Akhavidadegan et al. 2006)
Blood transfusion with infection complication	0.05	0.8	0.04	0.3	32	76	(Yang, Liu et al. 2017)
Operation duration >120 minutes with infection complication	0.05	0.8	0.22	0.55	33	84	(Bansal, Pawar et al. 2017)

2.9.6 Sampling Method and Subject Recruitment

The sampling method used to carry this study is simple random sampling. All patients underwent PCNL in HUSM are enrolled in this study.

2.9.7 Research Tools

The research tools proposal for the study entitled ‘A retrospective study on predictive risk of infection complication post PCNL in HUSM’ are as follows:

Firstly, the operation theatre book census. From this, all patients’ particulars (name and registration number) who underwent the PCNL procedure were obtained. The census is a reliable source of list of PCNL done in HUSM as it was manually entered by the surgeon or the assistant who did the operation.

Once the list of patients underwent PCNL was obtained, patient’s medical record will be traced from Medical Record Unit HUSM. The information acquired from this may include patient’s demographics (age, sex and comorbidity), the ultrasound KUB, CT urography, CT KUB and IVU report, the operative note, and urine culture report. If the information obtained from the medical record is not adequate or questionable, further information will be obtained from other source. For example, if urine culture not available in the medical record, it will be traced via the HUSM web (a recognized program run at USM to trace result) or traced directly from microbiology lab.

To identify the stone size and present of hydronephrosis, the report and image is available at ViaRAD4@10.1.6.22/10124@ZFP026 and <https://pacszfp.usm.my/zfp> respectively. These sites are used for references if the report not available as hard copy in the medical record.

A study pro forma is created to collect all the data required in this study. All the information obtained will be manually written by the researcher or research assistant on the study pro forma before the details entered into the SPSS system and analysed.

2.9.8 Operational Definition

1. Postoperative infectious complication carries wide range of definition. This includes:
 - 1.1. Postoperative fever with clinically significant of more than 38°C within hospital stay.
 - 1.2. patient experienced systemic inflammatory response syndrome SIRS according to the American College of Chest Physicians (ACCP) and the Society of Critical Care Medicine (SCCM) in 2001 (two or more positive of the following):
 - 1.2.1. body temperature >38°C or <36 °C,
 - 1.2.2. heart rate of >90 beats per minute,
 - 1.2.3. respiratory rate of >20 breaths per minute or partial pressure of arterial carbon dioxide (PaCO₂) <32mmHg,
 - 1.2.4. White cell count >12,000 cells/uL or <4,000 cells/uL.
 - 1.3. Sepsis was defined as both SIRS and evidence of infection present either positive blood culture or urine culture (Levy, Fink et al. 2003, Aghdas, Akhavizadegan et al. 2006, Rivera, Viers et al. 2016).

2. Diabetes mellitus defined as study participant who was diagnosed as diabetic with work-up show venous fasting blood sugar (FBS) more than 7.0 mmol/L or random blood sugar (RBS) more than 11.0 mmol/L or HbA1c more than 6.3% (Al-Qazaz, Sulaiman et al. 2011).

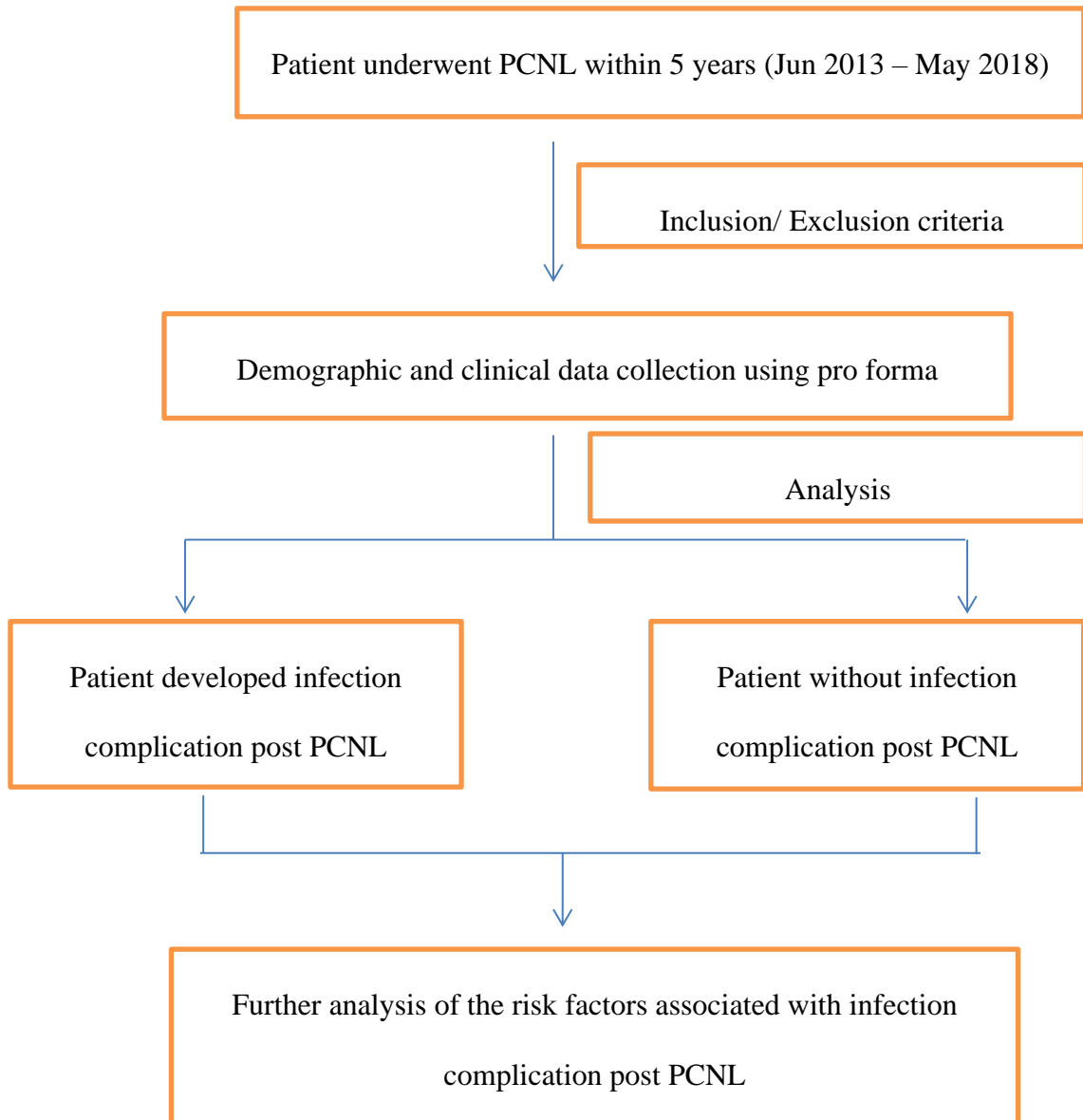
3. Hydronephrosis is defined as dilatation of the urinary collecting system of the kidney which includes the renal calyces, infundibula and renal pelvis. The grading of hydronephrosis is according to the ultrasound findings which can be divided into mild, moderate and severe (according to Society of Fetal Ultrasound, SFU system) (Fernbach, Maizels et al. 1993).

2.9.9 Data Collection Method

In this study, the information will be obtained by using the study tools. The data collection is done by using a study pro forma and carried out by the researcher or research assistant. The data collected will be kept and the researcher will maintain the confidentiality. The data collected will be kept until the data analysis is finished and the final research is submitted.

2.10 Study Flowchart

Figure 2.2: Study flowchart



2.11 Data Analysis

Data will be entered and analysed using Statistical Package for the Social Sciences (SPSS) version 22. Descriptive statistics will be used to summarize the socio-demographic characteristics of subjects. Numerical data will be presented as mean (SD) or median (IQR) based on their normality distribution. Categorical data will be presented as frequency (percentage).

The categorical variables were compared using Chi-square test. The unpaired *t*-test was used to compare the continuous variables between the groups. The simple logistic and multivariate binary logistic regression was carried out to find the significant factors associated with different outcomes. The $p < 0.05$ was considered significant.