DETERMINATION OF URINARY CALCULI COMPOSITION USING DUAL ENERGY CT

BY

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A dissertation submitted in fulfilment of the requirement for the degree of Master of Medicine (Radiology)

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ABSTRACT

To assess the incidence of the various types of urinary calculi composition using dual-energy CT (DECT). This study aims to determine the urinary calculi size, location, characteristics, and the radiation exposure for DECT KUB. It is a cross-sectional study performed from June 2018 until December 2019 at the Department of Radiology Hospital Tengku Ampuan Afzan (HTAA). Data of the patients that underwent DECT KUB protocol and had fulfilled the inclusion criteria were retrieved from the Radiology Information System (RIS). A total of 170 patients were selected using a purposive sampling method. The research featured 67% of males and 33% of females. Among the patients, 131 were Malays, 32 were Chinese, and 7 were Indians. The mean age was about 54.5. A total of 44 (26%) of urinary calculi was in the form of uric acid. Out of the 126, (74%) were non-uric acid type; calcium oxalate and calcium hydroxyapatite formed 78 (46%), and cystine constituted the remaining 48 (28%) of the urinary calculi. Most of the urinary calculi, with a total of 71 (42%), were less than 5 mm in size, and 77 (45%) were located in the lower pole of the kidney. The mean average of radiation exposure for DECT KUB was 11.5 mGy and ratio less than 1.1 classified as uric acid calculi, 1.1- 1.24 classified as cystine, and more than 1.24 classified as calcium. DECT KUB is not only highly sensitive and specific for urinary calculi diagnosis, but it can also characterize the urinary calculi chemical composition. This method could assist in medical intervention of urinary calculi (uric acid) that could be treated medically and may not require any surgery.

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 Medicine (Radiology)

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DECLARATION

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This dissertation is dedicated to my loving parents who have given and still giving their all, laying the foundation for what I turned out to be in life. To my supervisors and lecturers who have given a constant source of knowledge and inspiration.

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COMMON ABBREVIATIONS

HTAA	Hospital Tengku Ampuan Afzan
IIUM	International Islamic University Malaysia
PUJ	Prosedur Utama Jabatan
n	Number of Subjects Sampled

ABBREVIATIONS FOR POSTGRADUATE PROGRAMMES

CT	Computed Tomography
DECT	Dual Energy Computed Tomography
SECT	Single Energy Computed Tomography
KUB	Kidney, Ureter, Bladder
IVU	Intravenous Urography
eGFR	Estimated Glomerular Filtration Rate
CIN	Contrast Induced Nephropathy
SPSS	Statistical Package for the Social Sciences
US	Ultrasound
UA	Uric Acid
Non-UA	Non- Uric Acid
kVp	Kilovoltage Peak
mSv	Millisievert
DICOM	Digital Imaging and Communications in Medicine
RIS	Radiological Information System
PACS	Picture Archiving and Communication System
ESWL	Extracorporeal Shock Wave Lithotripsy
PCNL	Percutaneous Nephrolithotomy
MAG3	Mercaptoacetyltriglycine
HU	Hounsfield Unit
UTI	Urinary Tract Infection
PUJ	Pelviureteric Junction
VUJ	Vesicoureteric Junction
Z_{eff}	Effective Atomic Number
CTDIvol	Computed Tomography Dose Index Volume
DLP	Dose Length Product

INTRODUCTION

CHAPTER ONE

1.1 RESEARCH BACKGROUND

Urinary calculi is a very common health issue which contributed significantly to patient's morbidity and to the health care cost of patients (Smith et al., 1995). Patients typically experience intermittent flank discomfort, as well as urinary urgency, in addition to hematuria, nausea and vomiting (Curhan, 2007). If left untreated without proper treatment, obstructive urinary calculi most likely may cause infection to the obstructed urinary tract, subsequently becoming predispose to urosepsis, pyelonephritis, and ureteric strictures. Long-standing urinary obstruction will lead to renal insufficiency and may contribute to end-stage renal disease (Flohr et al., 2006). The options of urinary calculi treatment depend on its composition, which can only be decided once it had been removed. When this happens, it is too late to have an effect from any treatment decision henceforth (Heidenreich, Desgrandschamps & Terrier, 2002).

Urinary calculi imaging is done with the aim of establishing the presence of calculus in the urinary tract, assessing any complications, measuring the probability of calculus passage, validating calculus passage, as well as evaluating calculus burden and assessing disease activities (Dawoud et al., 2017). In recent times, the unenhanced helical computed tomography (CT) innovation has significantly increased the ability of medical providers to assess patients suffering from urinary calculus as it has been shown to provide information on the existence of calculus, size, and location (Heidenreich et al., 2002).

Computed tomography kidney, ureter, and bladder (CT KUB) is a rapid-non-invasive technique for urinary calculus diagnosis. It has been used in radiolucent calculus analysis. However, during its usage, CT has been able to show some significant features that makes it superior over intravenous urography (IVU) (Smith et al., 1995). This led to CT KUB being the first alternative to urinary calculi imaging. It has been found that, over the past two decades, its widespread use has almost surpassed IVU usage almost completely (Ahmed et al., 2010). Relative to other urinary tract imaging, CT KUB has been acknowledged as having certain distinct advantages for urinary calculi imaging. What makes it interesting is that it does not rely on the chemical composition of the calculus; with all calculus, except for the Indinavir calculus, are well seen. It does not involve contrast, and it can be conducted conveniently as it is employed in the preparation of surgical procedures (Sundaram & Saltzman, 1999).

On the other hand, single-energy CT (SECT) is unable to evaluate the urinary calculi chemical composition. To address this, dual-energy CT (DECT) was employed to evaluate the types of urinary calculus (Primak et al., 2007). It is acknowledged that DECT is definitely effective in distinguishing uric acid calculus from other calculus types with 92 percent up to 100 percent accuracy. The difference is in the size of calculus and attenuation of patients (Kaza et al., 2012). In addition, DECT not only provides excellent morphological details, it can also provide reliable and quantitative material information, which can be very functional in genitourinary imaging (Dawoud et al., 2017).

In an effort to discern urinary calculi components, DECT utilizes the discrepancy in calculi attenuation between low and high energy spectra (Primak et al., 2007). Through the DECT utilization, the classification of the urinary calculus can be determined either by evaluating the calculi attenuation ratio on low and high energy scans (dual-energy ratio on dual-source CT) or by calculating the effective atomic number (Z_{eff}) and contrasting such values to the attenuation profile or (Z_{eff}) of calculi with the established chemical composition (Kaza et al., 2017).

However, dual-energy CT is not routinely used in clinical practice. Thus, this study aimed at evaluating the dual-energy computed tomography's roles in the management of patients suffering from urinary calculi (Dawoud et al., 2017).

1.2 PROBLEM STATEMENT

This study would identify the most prevalent type of urinary calculus composition in Kuantan. To our knowledge, to this day, there is no similar study performed to establish the common types of urinary calculus among the population in Kuantan. The solitary readily accessible study found in Malaysia was carried out by Sreenevasan (1990), showing that non-uric acid calculi were the most common type of urinary calculus. Nevertheless, this study was conducted on a post-calculus removal examination based on chemical and crystallographic urinary calculi analyses. We hope that this study would be able to provide relevant evidence and data to further evaluate the efficacy and safety of DECT in evaluating and treating patients with urinary calculi.

1.3 RESEARCH OBJECTIVE

The objectives of this study are as follows;

1.3.1 General objective:

To describe the urinary calculus composition prevalence using dual-energy CT (DECT) (uric acid vs non-uric acid).

1.3.2 Specific objective:

i. To describe the sociodemographic characteristic of patients.
ii. To determine the distribution of types of urinary calculi.
iii. To measure the urinary calculi sizes.
iv. To establish the urinary calculi location.
v. To verify the radiation exposure for DECT in CT KUB.
vi. To identify urinary calculi characterization.

1.4 RATIONAL OF THIS STUDY

As pointed out in the above section, the treatment for the urinary calculi option relies on the composition of calculi. However, what is limiting is that it can merely be verified after it has been extracted. CT KUB has now become the first urinary calculi imaging option to replace IVU. It is recognized that CT is capable of detecting other unsuspected extra urinary and urinary abnormalities. Its capabilities makes it unique and outperformed other imaging techniques. In addition, although without contrast, all calculi were well seen on CT.

It has been found that dual-energy CT is effective in distinguishing uric acid calculi from other calculi types by 92 percent up to 100 percent precision (Kaza et al., 2012). In addition, the radiation exposure, according to the newest DECT protocols, is almost similar to single energy CT protocols from previous studies. Nevertheless, in urinary calculi imaging clinical practice, dual-energy CT is not routinely employed for that purpose. Thus, this study aimed at evaluating the dual-energy computed tomography's roles in treating urinary calculi patients.

1.5 ETHICAL CONSIDERATION

This study had been registered in the NMRR and was approved by MREC and other relevant authorities. This study number is NMRR id 18-1558-41612.

CHAPTER TWO

LITERATURE REVIEW

2.1 TYPES OF URINARY CALCULI

It has been reported that urinary calculi are formed due to the existence of the material deposition in circumferential layers around a central nidus. The central calculus nucleus composition may be different on the basis that the outer shell causes calculus production differences. The various material types accumulated around the nidus might be a result of many factors, for instance, urinary pH and diet, which can evolve with time (Prien & Prien Jr, 1968).

From an epidemiologic point of view, some authors mentioned the overall frequency of the components, whereas others identify them as their main components e.g., substance which accounts for more than 50% of the calculus (Daudon, Bader & Jungers, 1993). The chemical composition of uric acid calculus (composed of light elements such as hydrogen, in addition to carbon, nitrogen, and oxygen), calcium oxalate, calcium hydroxyapatite, cystine, and struvite calculus is made up of heavy elements namely phosphorus, calcium and sulphur (Primak et al., 2007).

Calcium oxalate monohydrate and calcium oxalate dehydrate are among the most prevalent compounds which can be found in the human urinary calculus. This constitutes over 80 percent of all urinary calculus (Schubert, 2006). Usually, 8 to 10 percent of the urinary calculus contains uric acid (Saw et al., 2000).

The calculus of calcium hydrogen phosphate dihydrate (brushite) is uncommon, which is, found to be less than 2 percent of urinary calculus. In 1-2 percent of calculi, cystine occurs uncommonly. The calculus of magnesium ammonium phosphate has been reported to be frequently correlated with alkaline urine, while urease splitting bacterial infections are accounted for approximately between 5 and 15 percent in humans (Dawoud et al., 2017).

Table 2.1 Chemical composition of common urinary calculi (adapted from Prien & Prien Jr, 1968)

Full Name	Abbreviation	Chemical Composition
Calcium oxalate monohydrate (whewellite)	COM	$CaC_2O_4.H_2O$
Calcium oxalate dihydrate (weddellite)	COD	$CaC_2O_4.2H_2O$
Magnesium ammonium phosphate hexahydrate	MAP	$MgNH_4PO_4.6H_2O$
Carbonate – apatite	CAP	$Ca_{10}(PO_4.CO_3OH)_6(OH_2)$
Hydroxyl – apatite	HAP	$Ca_{10}(PO_4)_6(OH_2)$
Calcium hydrogen phosphate dihydrate (brushite)	BRU	$CaHPO_4.2H_2O$
Uric acid	UA	$C_5H_4N_4O_3$
Cystine	CYS	$[-SCH_2CH(NH_2)-COOH]_2$

Table 2.2 Illustrates commonly occurring urinary tract calculi and describes their salient features (adapted from Kambadakone, Eisner, Catalano & Sahani, 2010)

	Composition	Frequency of Occurrence	KUB Radiographic Appearance	CT Appearance/Attenuation (HU)	Associated Etiologic Factors
	Calcium oxalate monohydrate and dihydrate (calcium oxalate dihydrate)	40%–60%	Radiopaque	Opacified/ 1700–2800	Underlying metabolic disorder (eg, idiopathic hypercalcuria or hyperoxaluria)
	Hydroxyapatite (calcium phosphate)	20%–60%	Radiopaque	Opacified/ 1200–1600	Usually no metabolic abnormality
	Brushite	2%–4%	Radiopaque	Opacified/ 1700–2800	. . .
	Uric acid	5%–10%	Radiolucent	Opacified/ 200–450	Idiopathic hyperuricemia or hyperuricosuria
	Struvite	5%–15%	Radiopaque	Opacified/ 600–900	Renal infection
	Cystine	1%–2.5%	Mildly opaque	Opacified/ 600–1100	Renal tubular defect

2.2 DUAL-ENERGY CT (DECT)

Dual-energy CT (DECT) has been developed and utilized widely since 2006. Currently, it comes with three different usable concepts. The first is focused on the two x-ray tube (dual-source imaging) technology that operates concurrently in 64 or 128-row detector scanners. The next concept is pertaining to dual-layer multidetector scanner device utilization with one X-ray tube conducting high-energy acquisition. Based on this concept, the top detector layer absorbs the majority of the low-energy photons (about 50 percent of the beam). On the other hand, higher-energy photons are absorbed by the bottom detector layer. Whereas, the third concept is in accordance with the utilization of a single X-ray source with rapid switching between two kilo-voltage settings (80 and 140 kVp) at 0.5 ms intervals. Through this configuration, during a single gantry rotation, it produces high and low-energy x-ray spectra (Kaza et al., 2012). DECT has been documented to have a sensitivity and specificity of almost 100% in the chemical composition characterization of the renal calculus with a size greater than 3 mm (Manglaviti et al., 2011).

A detailed evaluation of the composition of a calculus chemical can make it easier for clinicians to better fulfil the patient's treatment requirements. For instance, urinary calculi made of uric acid may be treated medically and may perhaps do not need to undergo surgery (William et al., 2003). The calculi location, in addition to size and amount, along with their chemical composition, does seem to be critical factors in the urinary calculi proper clinical management. For instance, cystine and monohydrate calcium oxalate calculi have a tendency to produce huge residual fragments that are challenging to remove (Dawoud et al., 2017). Renal calculus, which is less than 4 mm in diameter, can be discarded naturally in 80% of circumstances. Extracorporeal shock wave lithotripsy can be employed for 20 mm calculus; on the other hand, percutaneous nephrolithotomy or therapeutic ureterorenoscopy is utilized if the calculus' size is more than 20 mm (Dawoud et al., 2017).

In the clinical setting, the CT KUB initial preference over ultrasound should be tailored to the assessment of patients who are suffering from flank pain. Especially obese patients, evidently unwell or affiliated with gross/microscopic hematuria, are believed to be more likely to benefit significantly from CT scans. Conversely, it would be more relevant for vulnerable groups, such as children, pregnant women, and individuals who have a clinical diagnosis of musculoskeletal pain to initially be scanned with ultrasound (Moloney, Murphy, Twomey, O'Connor & Maher, 2014).

2.3 ADVANTAGE OF CT

CT KUB has been proven to be very fast in urinary calculi imaging without the need to use contrast compared to other imaging techniques (Cheng et al., 2012). In addition, CT KUB is highly sensitive for calculi detection of any size (Chelfouh et al., 1998).

The ability of CT to simultaneously detect other unsuspected extra urinary and urinary abnormalities has outperformed other imaging techniques (Smith et al., 1995).

Dual-energy CT, with its post-processing techniques, relies on urinary calculus chemical characteristics for the assessment of anatomical data, such as location, size, and calculus surface character (smooth or rough). A perfect breath-hold must be performed during image acquisition. This is in view of the usage of attenuation value to evaluate the chemical type of urinary calculi. An attenuation value obtained from images with slight motion differs significantly from those obtained without movement (Grosjean et al., 2008; Boll et al., 2009).

The goals of imaging in urinary calculi are to determine the presence of calculus accurately, to assess calculus composition, and finally to determine calculus size (Segura et al., 1997).

Patient's treatment will depend on the calculus size. A calculus of up to 5 mm has a 68 percent probability of passage, and a 5–10 mm calculus has a 47 percent probability of passage (Preminger et al., 2007). In addition, a study has shown that the calculi location needs to be included in the report as it will have an effect on the treatment. Generally, the more proximal the calculus within the ureter, the less likely it will spontaneously pass through (Coll, Varanelli & Smith, 2002).

2.4 ADVANTAGE OF CT KUB

It is well known that the European Society of Urogenital Radiology stated that an estimated glomerular filtration rate (eGFR) below 45 increases the contrast-induced nephropathy (CIN) risk. This is particularly true if there are additional risk factors, such as diabetic nephropathy and dehydration (Thomsen & Morcos, 2003).

It essentially precludes the use of enhanced CT KUB in such cases. In fact, CT KUB is beneficial in excluding urinary calculus and providing a definitive diagnosis of as much as 40 percent non-calculus obstruction (Shokeir et al., 2004). In the case of urinary calculi and obstruction assessment, CT KUB is commonly considered as the first-line imaging and is much preferable over IVU (Ahmed et al., 2010), owing to its high sensitivity and specificity that outperform other imaging modalities. It recorded a sensitivity value of 95 to 97 percent, specificity value of 96 to 98 percent and an accuracy value of 97 percent (Smith et al., 1996; Dalrymple et al., 1998).

In patients suffering from renal failure, it shows a higher value, which inhibits the use of intravenous contrast. Ultrasound sensitivity in ureteral calculus assessment and hydroureter detection is very low in comparison to CT KUB, which is approximately 46% and 50%, respectively (Ather, Jafri & Sulaiman, 2004). CT KUB could recognize 83% ureteral dilation, 80% hydronephrosis, 59% perinephric oedema, and 57.2% ipsilateral hydronephrosis (Ege et al., 2003). However, CT does not only reliably detects urinary calculi but as well as other triggers of flank pain. It encompasses both urinary and extra urinary abnormalities (Ather, Memon & Rees, 2005). Calculus from the vesicoureteral junction (VUJ), which sometimes passes through the urethra without significant changes in symptoms, can be diagnosed by careful CT inspection. However, CT KUB has limitations on being a non-contrast study. Enhancement or effects of infection and inflammation cannot be detected. Secondary signs of obstruction, such as perinephric, peri-ureteral, and unilateral hydronephrosis, are sometimes beneficial (Ather et al., 2004).

Planning for treatments includes a detailed preoperative evaluation of the size of the urinary calculus, the position and anatomical anomalies, including caliceal narrowing, the occurrence of the caliceal diverticulum, and much more. CT will be