Multiphase renal CT in the evaluation of renal masses: is the nephrographic phase necessary?

Nor-Azalina Songiwa, Mohammad Nazriib, Nur Adura Yaakupib, Hazman M. Norib, Zhonghua Sunb,c,*

a University of Malaya Research Imaging Centre (UMRIC), University of Malaya, 50603, Kuala Lumpur, Malaysia
b Department of Biomedical Imaging, Faculty of Medicine, University of Malaya, 50603, Kuala Lumpur, Malaysia
c Discipline of Medical Imaging, Department of Imaging and Applied Physics, Curtin University, GPO Box U1987 Perth, Western Australia, 6845, Australia

1. Introduction

According to the American Cancer Society, the prevalence of malignant renal tumors in general population is about 0.07% [1] with renal cell carcinoma (RCC) being the most common, which accounts for approximately 3% of adult malignancies. The incidence of RCC is increasing at an annual rate of approximately 2% [1]. This is partly due to the increased use of radiological imaging, which results in early detection of small asymptomatic lesions incidentally found during scanning for other conditions.

Standard four-phase helical renal computed tomography (CT) has been recommended and widely used in many clinical centers for detection and staging of renal tumors [2–4]. It includes preliminary phase (unenhanced phase), corticomedullary phase (CMP), nephrographic phase, and excretory phase (EP), corresponding to a scan delay of 30 s, 90 s, and 240 s at post intravenous (iv) contrast injections, respectively. Multiphase renal CT improves the sensitivity of renal lesions detection [5,6] but at the expense of increasing patient’s radiation dose, given the fact that CT is a high-dose modality [7–9]. Thus, it is important to reduce the number of CT phases in renal imaging, while still providing diagnostic images.

Studies have been conducted to reduce the number of phases used in multiphase renal CT without compromising image quality and ability to characterize renal lesions. A previous study by Yuh et al. reported that renal masses greater than 10 mm can be adequately assessed by EP [2]. Another study showed that nephrographic phase gave the least diagnostic information in the evaluation of renal lesions [3]. Gakis et al. showed that nephrographic phase was better than other phases in the detection of solid renal lesions; however, the CMP was found to be better for the lesion characterization [4]. It is a well-known fact that every additional phase in CT examination increases radiation dose to patients, thus increasing the risk of radiation-related malignancy. Therefore, this study was conducted to confirm the necessity of actual relevance of the nephrographic phase to the assessment of renal masses. We hypothesized that the nephrographic phase could be eliminated from the standard four-phase renal CT and that a three-phase renal CT may be suggested as a routine protocol, while the nephrographic phase can be done at a different setting if deemed necessary.

2. Materials and methods

2.1. Patient population

This study was approved by the local ethical research committee, and written informed consent was obtained from all patients before undergoing the procedure. Thirty adult patients aged above 30 years old (age range: 35–85 years old, mean±S.D.: 64.2±12.0) with suspicious renal masses detected either clinically or from other radiological imaging were prospectively collected from December 2008 to February 2011 at the University of Malaya Research Imaging Center, Kuala Lumpur, Malaysia. There were 20 males and 10 females. The presenting symptoms were variable among these patients with 7 (23%) patients presenting with microscopic hematuria, 3 (10%) with gross hematuria, 4 (13%) with loin pain, and 5 (17%) with loin pain associated with microscopic hematuria. Eleven (37%) patients were incidentally noted to have renal lesions on ultrasound performed for...
nonurological-related symptoms. Patients with congestive heart failure or chronic renal parenchymal disease were excluded from this study.

2.2. Four-phase CT scanning protocol

All patients underwent a four-phase contrast-enhanced multi-phase renal CT examination using the 16-slice multidetector CT scanner (16×0.75 mm, Siemens Medical Systems, Muenchen, Germany) with a tube current of 300 mA and tube voltage of 120 kVp. One hundred twenty milliliter of low osmolar nonionic contrast medium (iodine concentration 300 mgI/ml) (Iopromide, Schering, Berlin, Germany) was injected at an injection rate of 4 ml/s. Four-phase scanning was performed including a preliminary phase, CMP at 30 s, nephrographic phase at 90 s, and EP at 240 s post contrast injection. Each phase was saved in 5-mm slice thickness in different files and evaluated separately. The images obtained were also saved in two different sets, with one dataset containing all four phases (preliminary, corticomedullary, nephrographic, and EPs) and another dataset of three phases comprising preliminary, corticomedullary, and EPs (excluding the nephrographic phase). The value of each phase in the four-phase renal CT including the corticomedullary, nephrographic, and EP in the detection and characterization of renal lesion as well as renal parenchyma and renal vein opacification were assessed.

2.3. Characterization of renal lesions

The number of lesions detected in each phase and the size and location of the lesion either in the renal cortex or medulla were documented. Lesions were grouped into four different sizes: <10 mm, 10–30 mm, 30–50 mm, and >50 mm. Lesions sized less than 10 mm were included for lesion detection but were excluded for characterization due to its small size that can cause diagnostic difficulty. Lesions sized 10 mm and larger were assessed in terms of lesion's margin; wall thickness; the component of the lesion such as cystic, fatty, solid or mixed; the enhancement pattern; and the lesion attenuation (Hounsfield unit, HU) in three-phase and four-phase CT protocols. Lesion attenuation was measured with attempt to maintain the region of interest area at a size of at least 10 mm², at center of the lesion or the most homogenously enhanced part of the lesion. For lesions poorly depicted in any of phases, the location where lesion was seen on other phase images was used. Cystic lesions were characterized according to Bosniak classification. The diagnostic criteria for renal malignancy included a solid lesion or a complex cystic mass with thick irregular septa, thick calcifications, irregular inner wall, or presence of solid component. A scoring system is given to characterize these lesions into benign, indeterminate, or malignant.

2.4. Image interpretation and assessment

Image interpretation and measurement of attenuation for all scans were performed independently by two reviewers who had at least 4 years of experience in abdominal radiology. For lesion detection, the reviewers independently analyzed images from each phase (unenhanced, corticomedullary, nephrographic, and EP) separately and blindly within at least a 1-week interval to minimize bias. For lesion characterization, scans were interpreted during two different sessions within at least a 1-week interval. During the first session, a four-phased CT, combining unenhanced, corticomedullary, nephrographic, and EPs, was read, and during the second session, a three-phased CT, combining unenhanced, corticomedullary, and EPs, was evaluated. Interpretation discrepancies were resolved by consensus discussion. Conspicuity of each focal lesion was evaluated qualitatively and quantitatively on images obtained from each scan phase. Qualitative assessment was evaluated using a 5-point scoring scale to classify lesion conspicuity: score 0 = nonvisualized; score 1 = poorly visualized; score 2 = fairly visualized, that is, adequately shown but with poor delineation of margin; score 3 = good conspicuity with delineation of almost the entire margin; and score 4 = excellent conspicuity with clear demarcation of the entire margin. Standard reference images for grading were preselected and provided to each radiologist (Fig. 1).

![Reference images for visual conspicuity grading of renal lesion (arrow). Score 1: (A) poorly visualized lesion; score 2 (B) lesion adequately visualized but with poor delineation of margin; score 3: (C) good lesion conspicuity with delineation of almost the entire margin; score 4: (D) excellent lesion conspicuity with clear demarcation of the entire margin.](image-url)
The reviewers were allowed to change the preset window width (350 HU) and window level (50 HU) while viewing the images. A subjective scoring was assigned for each lesion on each scan phase and recorded into a standard format table. Quantitative measure-
ment of lesion conspicuity (LCQ) was defined as the difference between the attenuation values of the lesion from the surrounding parenchymal attenuation.

2.5. Radiation exposure

CT dose length product (DLP) was provided by the scanner console. Effective radiation dose was calculated by multiplying the DLP of the abdominal scan by a conversion coefficient (k=0.014 mSv/mGy/cm) [10,11].

2.6. Statistical analysis

Statistical analysis was performed with statistical software package [Statistical Package for the Social Sciences (SPSS) version 17.0 for Windows, SPSS Inc, Chicago, IL, USA]. The nonparametric Friedman test was applied to examine intergroup differences among the three scan phases for renal parenchyma enhancement, renal vein enhancement, and the qualitative and quantitative lesion conspicuity grading. The Wilcoxon signed rank test was used to compare the differences between three-phase and four-phase renal CT protocols in the detection and characterization of renal lesions. A P value of less than .05 was considered to indicate a statistically significant difference.

3. Results

Multiphase CT examination was successfully performed in all 30 patients without any complications. From the 60 kidneys evaluated, there were 118 renal lesions detected in both the three-phase and four-phase renal CT scans. Out of these lesions, 58 were smaller than 10 mm, and 60 lesions were measured 10 mm or more. The lesions that were 10 mm or larger were evaluated for lesion conspicuity and characterization. Ten lesions were classified as malignant (5 solid lesions and 5 complex renal cysts), 7 angiomyolipomas (AMLs), 2 solid lesions, which may represent benign lesion or lymphoma, 1 focal area of hypoperfusion (shown on CT as a focal, wedge-shaped noncontrast-enhanced region in the renal cortex), and 40 renal cysts (22 Bosniak 1, 16 Bosniak 2, and 2 Bosniak 2F). Of these 60 renal lesions, 35 (58.3%) were located in the renal cortex, and 25 (41.7%) were located in the renal medulla.

3.1. Renal parenchyma and renal vein enhancement

The cortical enhancement of the kidney was almost identical in all three phases with the highest enhancement noted in the CMP. The medullary enhancement reached the highest in the EP. The
enhancement of the renal cortex and medulla is almost equivalent in the nephrographic and EP with least difference seen in the EP, giving a more homogenous nephrogram in the EP (Figs. 2, 3). The renal vein enhancement reached the highest in the CMP. There is temporal decrease of renal enhancement from corticomedullary to EP (Fig. 3).

3.2. Lesion detection and conspicuity

There were only 9 (15%) lesions that were best visualized in the nephrographic phase, while 22 (36.7%) and 29 (48.3%) lesions were better visualized in the corticomedullary and EPs, respectively. There was significant difference of lesion conspicuity between corticomedullary or EP and the nephrographic phase (P<.05). All of the three phases (corticomedullary, nephrographic, and EP) were equally good in the detection of cortical renal cysts; however, the CMP was inferior to other phases in the detection of medullary cysts. In contrast, the CMP was the best in the detection of solid renal lesions (Fig. 4). All the three phases had almost similar ability in the detection of AML (Figs. 5, 6).

The CMP had the highest conspicuity value for the cortical lesions, though no significant difference was found between the three phases, and the EP has the highest conspicuity value for medullary lesions (Fig. 7).

3.3. Conspicuity and attenuation of malignant lesions

Of 10 malignant lesions, only 1 (10%) was best visualized in the nephrographic phase, while 3 (30%) and 6 (60%) lesions were best visualized in the corticomedullary and EPs, respectively. A significant difference of conspicuity of malignant lesions was found between the maximum conspicuity in either the corticomedullary or EP and the nephrographic phase (P<.05). The highest enhancement of malignant tumors was achieved in the CMP with washout seen in the nephrographic phase. EP gave the least tumor enhancement; however, there was no significant difference of the enhancement between the nephrographic and EPs (P>.05) (Fig. 8).

3.4. Four-phase versus three-phase renal CT protocols

All lesions detected in the four-phase renal CT were also detected in the three-phase renal CT with no significant difference noted (P>.05). There was also a good correlation between the four-phase renal CT and three-phase renal CT in characterizing renal lesions. No significant difference was reached for both sets of CT to characterize the renal lesions (P>.05). There was also no significant difference in degree of confidence of both reviewers in diagnosing renal lesions using either four-phase or three-phase renal CT (P>.05).

3.5. Radiation dose between four-phase and three-phase CT protocols

The mean DLP of four-phase CT and three-phase CT protocols was 1486 mGycm and 1164 mGycm, with corresponding effective dose...
being 20.8 mSv and 16.3 mSv, respectively. There is approximately 22% reduction of radiation dose when the nephrographic phase was excluded from the standard four-phase renal CT protocol.

4. Discussion

Multiphase renal CT has been widely used in characterization of renal tumors and preoperative staging of RCC due to its high sensitivity and specificity to detect and characterize the renal lesions [12–14]. A potential criticism to the four-phase CT protocol is an increase in radiation dose to the patient. This study shows that the routine four-phase renal CT can be replaced with a three-phase protocol with elimination of the nephrographic phase without compromising diagnostic ability.

A four-phase CT protocol is routinely used in the detection and diagnosis of renal lesions. Unenhanced scanning represents a baseline for measurement of lesion enhancement after iv administration of contrast medium. CMP is useful for detection of the renal arteries and vascular anomalies. Nephrographic phase allows maximal opacification of renal veins and staging of the renal disease, while EP has been reported as the important phase for detection and characterization of renal masses. With a delay of 4 min, EP demonstrates the advantage of simultaneous renal excretion and evaluation of the relation between the neoplasm and the collecting systems [15,16]. This analysis on renal enhancement showed that the cortical enhancement among all three phases is almost identical with the highest enhancement noted in the CMP. This is contrary to previous studies that showed that cortical enhancement was best seen in the nephrographic phase [13,17]. Results of this study indicated that the renal medulla was least enhanced in the CMP but demonstrated temporal increase with maximum enhancement in the EP. These findings can be correlated to the renal histoanatomical structures whereby the contrast flows into the filtering portion of a nephron located in the cortex followed by a renal tubule that passes from the cortex deep into the medullary pyramids, which later drains into the collecting duct. This probably also explains why cortical lesions were best demonstrated in the CMP and why medullary lesions were best demonstrated in the EP. The enhancement of the cortex and medulla is almost equivalent in the nephrographic and EP with least difference seen in the EP, giving a more homogenous nephrogram in this phase. Theoretically, any lesion occupying both cortical and medullary regions is best demonstrated in the EP.

This study was not confined to the evaluation of RCC but looked into various renal lesions, which were detected in the study population. Most of the patients were symptomatic, as this was the

Fig. 6. Four-phase renal CT shows left RCC (arrow) that demonstrates best tumor enhancement in the CMP (B), compared to other phases. A=plain CT, C=nephrographic phase, and D=EP.

Fig. 7. Lesion conspicuity of cortical and medullary renal lesions between different phases of renal CT imaging.

Fig. 8. Enhancement of malignant lesions during different phases of renal CT scans.
indication for a renal-specific CT scan. Although Schlimmer et al. noted that most small renal lesions are found incidentally, the article showed that they reviewed CT, ultrasound, and MRI investigations that were nonrenal specific [18]. Of 30 patients with a total of 118 lesions being detected, most of them were simple renal cysts accounting for approximately 89% of total lesions. Fifty-eight (49%) lesions were smaller than 10 mm, most of which were likely to be simple cysts, and 60 (51%) lesions were larger than 10 mm. From a clinical perspective, the CMP is less sensitive in detecting small renal lesions as noted in a previous study by Szolar et al. [6], in which the nephrographic and EPs were found to have similar ability in detecting small renal lesions measuring less than 10 mm. Again, results of this study confirmed the possibility of eliminating nephrographic phase without affecting detection of both small and large renal lesions.

The optimum enhancement of malignant tumors was best achieved in the CMP with maximum peak enhancement of 210 HU (mean = 146.7), as most of malignant lesions particularly RCC and urothelial tumors are hypervascular and enhanced early following iv contrast due to their supply by the renal artery [17,19]. Most of these lesions wash out during the nephrographic (maximum enhancement = 140 HU, mean of 111.6) and EP (maximum enhancement = 137 HU, mean of 94.2). This is consistent with the lesion conspicuity evaluation that showed significant difference of conspicuity of malignant lesion between the corticomedullary and the nephrographic phase (P < .05) as 90% of the malignant lesions were best visualized in the CMP while only 10% lesions were better visualized in the nephrographic phase. Tumor enhancement was the least in the EP due to contrast washout from the tumors in this delayed phase, which is consistent with a previous study [20].

The effective doses related to the four-phase and three-phase renal CT used in this study were 20.8 mSv and 16.3 mSv, which is significantly higher than that reported in a recent study by Tsilis et al. [21]. This is mainly due to the use of high tube current in this study, despite using tube current modulation. With recent multislice CT models of 64-slice and post-64, tube current modulation across the patient’s body during tube rotation is available with reduction of effective dose achieved satisfactorily [22–24].

The main limitation of this study was the small samples size with relatively low variants of renal pathology. This was due to the inclusion/exclusion criteria and patient willingness to participate in the study, as well as the general load of patients undergoing multiphasic renal CT in our center. Out of 118 lesions, only 60 lesions could be evaluated for characterization. Most of these lesions were benign cysts that contributed to most of the lesion conspicuity. There is no definitive biopsy performed—just consensus diagnosis from imaging based on enhancement appearances.

Another limitation is the suboptimal renal perfusion imaging that leads to different or delayed attenuation of the renal enhancement. This is due to the use of fixed scan delays for the four-phase renal CT protocol. A bolus-tracking technique has become widely available and has been increasingly used to optimize scan timing in individual patients to compensate for the variability of circulation time between patients. Goshimat et al. reported that the bolus tracking technique improved contrast enhancement in multiphasic renal CT imaging of the kidney and renal vessels as the scan delays were based on individual patients [25].

In conclusion, excluding the nephrographic phase from the standard four-phase renal CT protocol does not reduce the ability to detect and characterize renal lesions. Therefore, a combination of plain, corticomedullary, and EPs is adequate to assess renal lesions with the advantage of lowering radiation dose.

References