Quantitative Estimation of Urinary Tract Obstruction by Optical Density Evaluation of Fluoroscopic Images

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Abstract.
Evaluation of upper urinary tract obstruction is often performed by visual monitoring of sequential fluoroscopic imaging in order to estimate the clearance of the injected contrast media from the renal pelvis. However, the diagnostic accuracy of this method is debated due to its subjectivity. The purpose of this study was to develop a computerized method for quantitative evaluation of the upper urinary tract clearance rate, using conventional fluoroscopic images. The quantification of the clearance rate was based on measurements the radio density of the contrast media in the renal pelvis compared to that of a radiological phantom attached to the patients during the measurement. The method was tested by analyzing 31 patients following percutaneous nephrolithotomy (PSNL) and retrograde or antegrade pyelography. 26 patients were considered non-obstructed and 5 were diagnosed as obstructed. The obtained clearance curves highly fitted an exponential regression curve with a correlation coefficient of R=0.94±0.02 . This correlation prevailed over a wide range of time (from 3 min to 30 min) and over a wide range of the amount of contrast media. Normal clearance was found at rate greater than 8.3% per minute. In obstructed cases the maximal clearance rate were found 2.64% per min. The average clearance rate of the non- obstructed patients was about 7 times higher than that of the obstructed patients. It was concluded that the relative clearance rate may provide an accurate quantitative estimation of the upper urinary tract obstruction using only the initial diagnostic phase of a routine urological modality.

Introduction

Obstruction of the upper urinary tract is a common urological pathology that results from obstructing stones, tumor or UPJ stenosis. Patients with this pathology are being evaluated with intravenous urography, retrograde or antegrade urethrography using sequential X-rays imaging to evaluate the contrast media clearance from the upper urinary tract as a clue for obstruction [1,2]. Modern clinical X-ray imaging devices are digital and can be utilized for quantitative analysis of contrast media clearance from the upper urinary tract. The purpose of this study is to evaluate feasibility of the method that will enable a quantitative estimation of the degree of upper urinary tract obstruction, using conventional in urological practice equipment for retrograde or antegrade pyelography. The study is based on the known dependences between the clearance of a substance and the time constant that describes its removal rate [3] and based on the hypothesis that the degree of upper urinary tract obstruction can be described quantitatively by contrast media clearance from the renal pelvis. This can be performed by analyzing the time dependence of the contrast media radio-density measured in sequential X-ray images using different radiological techniques [4-6]. In this study we examined the feasibility of the method using conventional in urological practices X-ray fluoroscopy and semi quantitative densitometric approach [7]. When referring to the function of the kidney, clearance of a substance is the inverse of the time constant that describes its removal rate divided by its volume of distribution. Renal clearance can be measured in steady state conditions with a timed collection of urine and an analysis of its composition. The dependence of urea clearance on urine flow rate was modeled theoretically and was studied and fitted to human data [8] at an average urine flow rate of 1.5 ml/min. Modern modification and application of this model for dialysis was also described [3]. It is assumed that a differential equation, which models homogeneous concentration of urea, is applicable to describe the contrast media clearance in the renal pelvis. Using this assumption, the clearance equation can be written as:

$$V\frac{dC}{dt} = -Q \cdot C \ , \qquad (1)$$

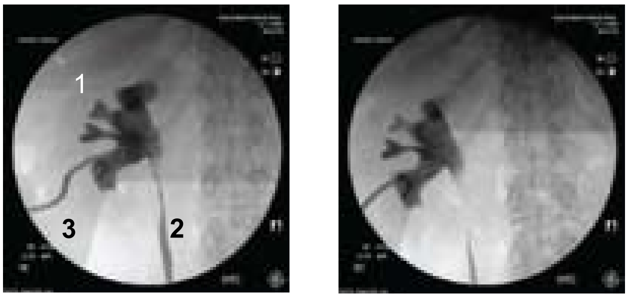
where V is the volume of the renal pelvis, Q is the average urine flow in ml/sec and C is the average concentration of the contrast material in the pelvis in mg/ml. According to the indicator–dilution approach [6], equation (1) shows that the radio-density of the renal pelvis can be described by an exponent as function of time (clearance curve). Therefore, the value of the relative clearance rate $K = Q/V$ (percentage volume of the contrast material leaving the renal pelvis per time unit) can be estimated experimentally by using exponential fitting of the measurements of the pelvis radio-density as a function of time. The value of K can be calculated as the inverse value of the time constant in the exponent.

Digital imaging, which allows repetitive density analysis of the same region of interest (ROI) during the transit of contrast media, holds a potential to estimate the dynamic characteristics of contrast dilution curves. This method, which is based on digital X-ray subtraction angiography (DSA) has numerous advantages for the diagnosis, monitoring and quantitative evaluation of blood flow and velocity in cardiologic practice [6]. However, temporal subtraction in cases of upper urinary tract sequential X-rays imaging is more complex due to the long time interval (minutes) between the two subtracted images. Patient positioning and body habitus differences between images acquired during urinary tract imaging make DSA problematic for being used in urography practice [2]. Parametric images have been used widely in nuclear medicine, and somewhat more sparingly in X-ray CT. Gallagher and coauthors [9] have used parametric images to distinguish between transplant kidney rejection and acute tubular necrosis using renal images obtained from digital fluoroscopy. Hackstein and coauthors [10] present a technique to measure kidney clearance of the applied contrast media by multiphase helical CT by measurements the time density curve of the kidney after contrast media application.

In the present study the optical-density of the contrast material in regular X-ray video-fluoroscopy was measured as a function of time, in order to evaluate the upper urinary tract clearance rate. This was performed by analyzing the time dependence of the contrast media radio-density measured in sequential images of the whole renal pelvis area. The indicator–dilution approach (Stewart-Hamilton method) and the first-pass distribution analysis [11,12] are well investigated for blood flow and velocity measurements, and we assumed that these methods can be also used to calculate the contrast media clearance rate.

2 METHODS

Antegrade or retrograde urethrography studies were performed with a mobile C-Arm model BV29 (Phillips) and C-Arm model OEC 9900 Elite (GE Healthcare). The sequences of the urethrogram were captured after injection of the contrast media (Telebrix® 30M, 300mgJ/ml, Guerbet Corp.) by using the "last-frame-hold" at 3 frames per second, with 2 frame averaging using AGC and ABC modes of the C-Arms. Figure 1 displays digital fluoroscopic images of the right kidney, captured during upper urinary tract examination.



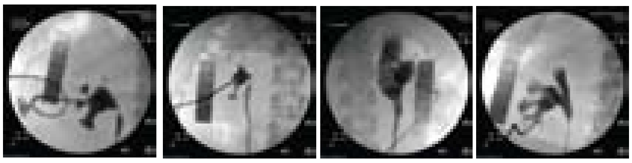
1a **1b**

Figure 1. Fluoroscopy images obtained during upper urinary tract examination (1- the contrast agent in the renal pelvis, 2- the ureter, 3-neprostome). Figure 1a shows the initial stage of the pyelography, in which the injected contrast agent was already transported by the urine to the ureter. Figure 1b demonstrates the next stage of the examination, in which both the radio-density of the contrast agent and the area it occupies are reduced.

A total of 31 patients (16 males, 15 females) were included in the study. Patients who underwent kidney surgery, kidney implantation, anatomical dysfunction and patients suffering from renal diseases were excluded. 26 patients were considered non-obstructed and 5 patients were diagnosed as obstructed (2 after PCNL with UPJ obstruction, 2 nephrostogram due to obstruction of ureter and 1 retrograde urethrography due to UPJ obstruction). The diagnosis was established by experienced urologist and was based on case history and following ultrasonography and CT examinations.

Image processing prior to image analysis included image enhancement in order to perform automatic tracing of the renal pelvis and image segmentation. In some cases, spatial calibration and image registration was also utilized. The image measuring algorithm included analysis of the electronic noise and analysis of the X-ray scattered radiation.

In order to estimate the amount of the contrast agent in the acquired images, the semi-quantitative densitometry approach was utilized. A logarithmic transformation of the system response was performed for scaling image data to optical density values. Subtraction of the background optical density was used to remove the soft tissue and the X-ray scattered radiation from the image. Linearization of the system response was performed by using the radiological wedge (phantom) which was attached to the patients during the examination. The measurements were performed on ROIs which included the contrast agent in the renal pelvis, reference regions the radiological wedge and reference regions of background.



79kV 82kV 92kV 98kV

Figure 2. Examples of fluoroscopy images captured during clearance studies of 4 different patients with 4 different X-ray tube voltages, shown at the bottom of each image. The radiological wedge which was placed next to the renal pelvis can be seen in the FOV of the image intensifier.

The radio-density of the contrast agent was measured in arbitrary units for all the fluoroscopy images acquired during clearance study. The image measurements and data processing were verified using phantom-based modeling experiments, which simulated a clearance study of the upper urinary tract. The accuracy of the relative changes in the radio-density measurement was estimated by a dynamic radiological phantom, which was developed for simulating an antegrade urethrography study and was found to be ±3%. Clearance curves were generated to describe the relative changes of the radio-density of the renal pelvis as a function of time and the clearance rate was calculated using the exponential fitting of these curves.

Clearance curves approximated by a decreasing exponent were analyzed for the 31 patients. The Pearson's correlation coefficients of the exponential approximation were obtained by regression analysis and the time constant was calculated for each curve. The relative clearance rate *K* was calculated for each patient as the inverse value of the time constant in the exponential clearance regression curve.

To examine our assumption, that for non-obstructed cases the clearance curve can be described by the decreasing exponential function, all the values of radio-densities, which were measured for the 26 non-obstructed patients, were grouped into one data array. This array was reordered as function of $t/\square$ where t is the time from the beginning of the clearance study, and $\square$ is the value of the calculated time constant for each patient, and fitted by a decreasing exponent. To estimate the feasibility of this method in urological practice the distribution of the clearance rate values and the distribution of time constant values were analyzed for 26 of non-obstructed patients.

Results

The obtained clearance curves for all of non-obstructed patients highly fitted an exponential regression curve with a correlation coefficient of $R=0.94\pm0.02$. For the 5 patients with urinary tract obstruction, the clearance curves also showed exponential regression fitting with a lower correlation coefficient of $R=0.86$. These curves showed a slow decrease of the pelvis radio density with time. Those correlations prevailed over a wide range of time (from 3 min to 30 min) and over a wide range of the amount of contrast media.

Figure 3 shows a scatter diagram of the experimental data (relative changes of the pelvis radio density as function on time) for all the studied cases. The white dots on the plot represent normal cases and the black dots represent obstructive cases. The solid line shows the mean clearance curve for the normal cases, as calculated by the geometric mean values of the experimental data.

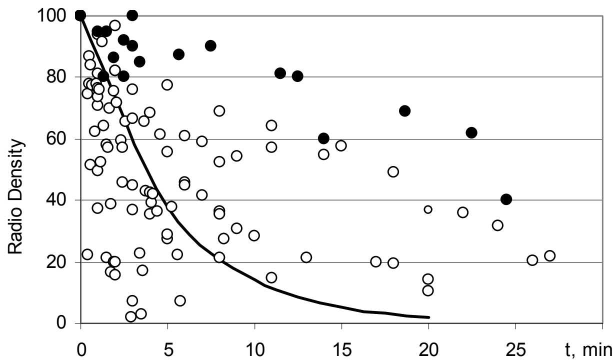


Figure 3. Experimental data of the relative changes the pelvis radio-density as function on time for all studied cases. White and black dots on the plot represent normal and obstructed cases, respectively. The solid line represents the mean clearance curve for the non-obstructed cases.

For the obstructed cases the minimal time constant - τ, which were observed was 37.9 min and the maximal clearance rate - K was 2.64% per min. For the non-obstructed cases, the mean time constant τ was 5.1 min and mean clearance rate was 19.6% per min. The results for the non-obstructed and the obstructed patients in the present study did not overlap. The maximal time constant found for the patients, who were considered non-obstructed, was 34.2 min and the corresponding minimal clearance rate was 2.9% per min.

Figure 4 shows a scatter diagram of the relative changes the pelvis radio density in the non-obstructed patients (26 cases) as a function of time in normalized units (t/τ), where t is the time from the beginning of the clearance study, and τ is the value of the calculated time constant for each patient.

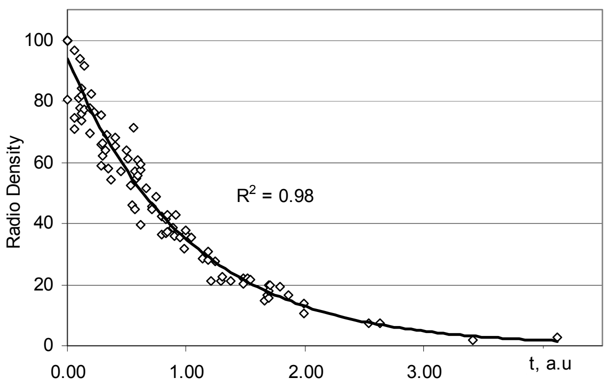


Figure 4. The relative changes the pelvis radio-density in the non-obstructed cases as a function of time in normalized units (t/τ). The solid line represents the resulting exponential regression curve.

This figure shows that the relative changes in the radio-density of the renal pelvis correlated extremely well by an exponential regression curve. The high correlation was observed over a wide range of time (up to 3τ).

Discussion

In this study the feasibility of measuring the contrast media clearance from the renal pelvis for diagnosing upper urinary tract obstruction was examined. This was performed by analyzing fluoroscopic images of contrast media in the pelvis, and measuring the optical density of the pelvis as a function of time. Relative clearance curves of the contrast media were obtained, and the urine flow (through the ureter) was estimated by calculating the relative clearance rate K. The obtained clearance curves highly fitted an exponential regression curve with a correlation coefficient of R=0.94.

The clearance rate for the normal cases was found to be greater than 8.3% per minute, with a mean of 19.6% per min. For the obstructed cases, the maximal clearance rate was only 2.64% per minute. The mean time constant for the normal cases was 5.1 min, while the minimal time constant for the obstructed cases was more than 7 times higher - 37.9 min. These results suggest that only two routine urethrography images, with 5 min interval, may be sufficient for diagnosing upper urinary tract obstruction by a quantitative estimation of the urine flow rate through the ureter.

The concept of using urethrography studies for obtaining quantitative information regarding upper urinary tract dysfunctions, has many advantages. The described method does not depend on patient body position or on body habitus, and the clearance rate of the contrast material is expressed quantitatively, allowing for accurate follow-up of patients. Moreover, since the clearance rate can be determined at the very early stages of the fluoroscopy examination, the exposure dose of the patient to ionizing radiation is significantly reduced. Furthermore, the method can be modified using the real-time DSA approach and hold a potential for measuring the clearance rate in absolute units (ml/sec) and for assessing the inhomogeneity of the urine generation in the different regions of the kidney.

The main limitations of the present study are the small number of cases studied and the fact that the data processing is currently laborious in the absence of automated software. However, compared to visual monitoring of the contrast flow through the ureter performed currently, quantitative measurements of the radio-density of the renal pelvis could provide an accurate estimation of the relative clearance rate. This method provides a quantitative estimation of the upper urinary tract obstruction using only the initial measurement phase of a routine urological modality, without additional CT examination, additional contrast injection, and additional radiation exposure.

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Prof. Isaac Leichter PhD

Prof. Leichter completed his B.Sc. in physics and mathematics in 1970 and his MSc in physics, *with distinction*, in 1975, at the Hebrew University. He earned his PhD in Physics at the Hebrew University in 1982, implementing the Compton Effect as a diagnostic tool in medicine. Prof. Leichter completed postdoctoral fellowships in medical physics at the University of California, Los Angeles in 1982-1983 and at the Hebrew University in 1984-1986. In 1983 he joined the Department of Applied Physics at the Jerusalem College of Technology (JCT) as a senior lecturer and the Department of Diagnostic Imaging at Hadassah Medical Center as the department physicist and senior physicist in radiology research. Since 1993, he is an Associate Professor and the Head of Medical Engineering Program at JCT.

Prof. Leichter has conducted extensive research on the early diagnosis of metabolic bone diseases by radiographic methods for measuring bone density, and on estimating fracture risk by spectral analysis of digital radiographs. In recent years, his research has focused on computer-aided radiographic techniques for the detection and evaluation of breast cancer, lung nodules and upper urinary tract obstruction, as well as on spectral characterization of human tissues and material separation with dual-energy computed tomography.