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Research article

Improvement of allograft kidney biopsy yield by using a handheld smartphone microscope as an on-site evaluation device

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ABSTRACT

Background: Smart lens is a magnifying device that turns the smartphone into a microscopic exploring instrument. It is a convenient and inexpensive tool as an on-site evaluation device for the kidney biopsy specimen. We demonstrate the benefit of using a handheld smartphone microscope compared to the standard procedure in allograft kidney specimens.

Material and methods: This was a cohort study of allograft kidney biopsies performed between June 2015 and November 2017 in Srinagarind Hospital, Khon Kaen University, Thailand. The clinical utility of the "Chula smart lens" applied to the smartphone as an on-site evaluation device was studied. Clinical data, diagnostic quality, and complications were retrospectively reviewed and compared between the smart lens group and the standard group.

Results: The study cohort consisted of 93 allograft kidney biopsies (standard:47, smart lens:46). The mean age was 40.6 (18–48) years, and 63 patients (67.7%) were male. By using the smart lens device, the number of obtained tissue cores was higher (3.5 vs 2.9, $p = 0.019$) and the inadequacy rate for diagnosis was significantly lower (7% vs 21.3%, $p = 0.05$).

Conclusion: Using a handheld smartphone microscope as an on-site evaluation device resulted in more positive glomeruli and diagnostic yield compared to the standard procedure.

1. Introduction

Kidney transplantation is an important procedure in renal replacement therapy for end-stage kidney disease patients [1]. It was shown to prolong survival and improved the quality of life of the patients [2, 3]. Despite significant progress, medical and surgical complications after the surgery can happen.

A percutaneous kidney biopsy is a common and essential tool for evaluating medical renal diseases and determining allograft survival [4]. The pathological results of the kidney biopsy specimen could change the course of treatment and result in preserving the transplanted kidney [5]. However, it is an aggressive procedure with many possible complications such as gross hematuria, perirenal hematoma, arterio-venous fistulas, and wound infection. Some complications following kidney biopsy may need invasive intervention like embolization or graft nephrectomy. Thus, balancing the risk and benefit of the procedure is crucial.

Inadequate specimens could result in a delay in diagnosis and treatment which could jeopardize the function of the allograft. Moreover, the repeated biopsy further put the patient at risk for more complications and increased health-care costs [6].

The adequacy assessment evaluated by the on-site microscope was found to be effective in improving both native and allograft biopsy adequacy [7, 8, 9]. Nevertheless, it is a complex procedure that involves the increase of man-hours. Therefore, it is not widely accepted and is not routinely done in many centers [8, 9].

The incorporation of the lens into the smartphone has turned this combination into a portable microscope. Several smartphone-based microscopes have been used in detecting detailed images such as human cells and parasites [10, 11, 12, 13].

In this study, we evaluated the use of a Chula smart lens magnifying device with the smartphone to screen the quality of kidney transplanted specimens and compared the results with the standard procedure done in the institute.

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2. Material and methods

2.1. Study design and cohort

This study was a retrospective study of a prospective cohort that included adult patients (≥18 years old or older) who underwent percutaneous allograft kidney biopsy in Srinagarind Hospital, Khon Kaen University (KKU). Srinagarind Hospital is a large university hospital that conducted kidney transplantation in approximately 60 cases per year.

The indications for allograft biopsy were 1) unexplained increase in serum creatinine, 2) serum creatinine has not returned to baseline after treatment of acute rejection, 3) expected kidney function is not achieved within the first 1–2 months after transplantation, and 4) new onset or unexplained proteinuria.

2.2. Instrument

A portable smartphone microscope, the integration of a 40x magnification "Chula Smart Lens" " (available on http://chula-smartlens.lnwshop.com/, price: THB650 or USD 22 (May 2021) and a smartphone, was developed for on-site evaluation of the biopsy samples. The device was tested with the kidney biopsy specimens to ensure its ability to detect glomeruli.

2.3. Procedure

All percutaneous allograft kidney biopsies were performed by urologists under ultrasonic guidance with local anesthesia and the use of a 16-gauge needle. After the procedure, vital signs were monitored, and all patients were observed for complications for at least 24 h.

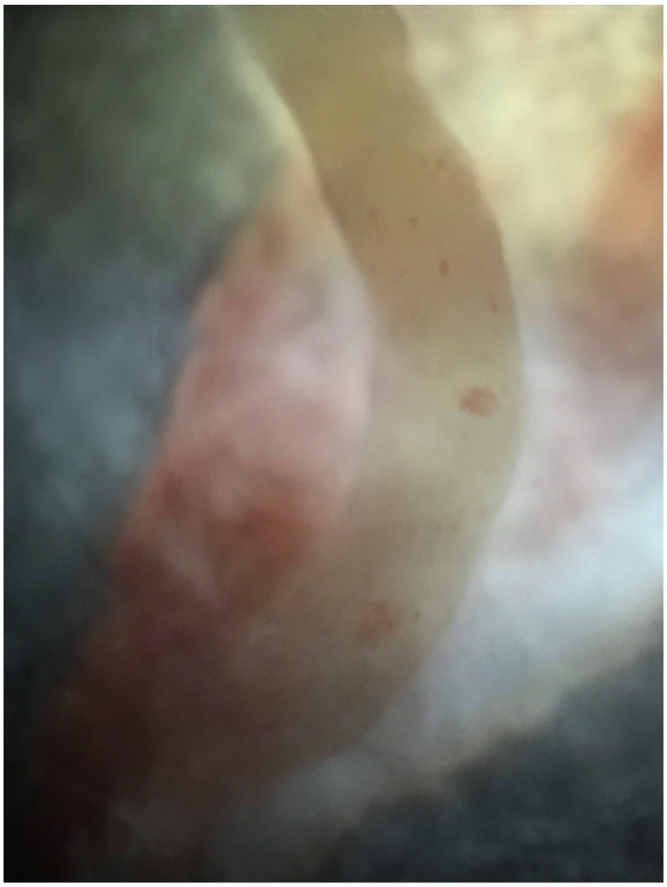

Figure 1. A picture of a glomerulus in the tissue core via the smartphone microscope.

Patients were classified into the "Smart lens group" if the biopsies were evaluated by an on-site smartphone microscope. For other patients, they were classified into the "Standard group". At least one glomerulus detected on a handheld smartphone microscope (Figure 1) by the urologist who performed the biopsy was considered adequate before proceeding to the pathology department. Baseline characteristics, laboratory investigations, pathological reports, and peri-operative complications were collected.

2.4. Statistical analysis

Demographic data were analyzed using descriptive statistics and presented as percentage, mean, and standard deviation. If the distribution did not conform to the normal distribution, median and interquartile ranges were used. For all statistical comparisons, a p-value of <0.05 was considered statistically significant. All data analysis was carried out using STATA software version 10.0 (StataCorp, College Station, TX, USA).

2.5. Ethical consideration

Ethical approval was provided by the Khon Kaen University Faculty of Medicine Ethics Committee as instituted by the Declaration of Helsinki (reference number HE601474). All data was anonymized and maintained with confidentiality. The patient consent to review the medical record was not required due to the retrospective nature of the study.

3. Results

3.1. Baseline characteristics

Between June 2016 and November 2017, a total of 93 kidney transplanted patients were enrolled in this study: 47 patients in the standard group and 46 in the smart lens group.

Table 1 shows demographic data and comorbidity conditions at baseline. The mean age was 40.4 years among patients in the smart lens group and 40.8 years among those in the standard group. Overall, 63 (67.7%) of the patients were men and 75 (80%) patients were diagnosed with hypertension.

3.2. Laboratory and ultrasonographic findings

The baseline hematocrit and glomerular filtration rate levels were comparable between the two groups as shown in Table 2. The skin to kidney distances was slightly higher in the smart lens group, on the contrary, the renal cortical thickness was higher in the standard group.

3.3. Kidney biopsy outcomes

The mean number of core tissues obtained from the biopsy was significantly higher in the smart lens group compared to the standard group (3.5 vs 2.9 glomeruli, $p = 0.019$) as shown in Table 3. Moreover, the proportion of positive glomeruli (at least one glomerulus in the sample) was significantly higher in the smart lens group (100% vs 83%, $p = 0.005$). The inadequacy rate for diagnosis was significantly higher in the standard group compared to the smart lens group (21.3% vs 7%, $p = 0.05$).

More patients in the smart lens group developed gross hematuria (15% vs 2%). None of the patients in the study suffered from perirenal/perinephric hematoma, hypotension, or renal arteriovenous fistulas.

Table 1. Details of 93 patients who underwent transplanted kidney biopsy.

Patients	All biopsies	Smart lens group	Standard group	p-value
Number of patients	93	46	47	
Age (year)				
Mean (SD)	40.6 (14.8)	40.4 (15.6)	40.8 (14.2)	
Range	18–68	18–68	18–67	0.90
Sex, n (%)				0.16
Male	63 (67.7)	28 (60.9)	35 (74.6)	
Female	30 (32.3)	18 (39.6)	12 (25.5)	
Transplantation to biopsy interval (month)				
Median (IQR)	28 (1.1, 123.9)	63.5 (3.7, 129.7)	11.4 (0.9, 63.5)	0.04
Body mass index (kg/m^2)				
Median (IQR)	21.2 (18.7–23.7)	21.9 (18.9–24.2)	20.6 (18.5–23.2)	0.43
Antiplatelet or anticoagulant use, n (%)	6 (7)	2 (5.3)	4 (8.5)	0.56
Hypertension, n (%)	75 (80.6)	36 (78.3)	39 (83)	0.61
Diabetes, n (%)	11 (11.8)	6 (13)	5 (10.6)	0.76
Hepatitis virus infection, n (%)	5 (5.4)	3 (6.5)	2 (4.3)	0.68

SD: standard deviation, IQR: interquartile range.

Table 2. Laboratory and ultrasonographic findings at baseline.

Patients	All biopsies	Smart lens group	Standard group	p-value
Laboratory values				
Hematocrit (vol%)				
Median (IQR)	30 (27–34.1)	30 (28.7–34)	30 (26–34.1)	0.59
Platelet count ($10^9/L$)				
Mean (SD)	231 (74.2)	238 (73.8)	224 (74.6)	0.36
INR				
Mean (SD)	1.02 (0.08)	1.02 (0.07)	1.01 (0.08)	0.32
Creatinine Clearance[a](mL/min)				
Median (IQR)	27.5 (20.4–37.0)	25.8 (19.4–41.2)	27.9 (20.4–35.6)	0.76
Ultrasonographic findings				
Parenchymatous change[b], n (%)	37 (43.5)	18 (41.9)	19 (45.2)	0.75
Skin to kidney distance (cm)				
Median (IQR)	1.3 (0.9–1.7)	1.3 (0.9–1.5)	1.2 (0.9–1.9)	0.69
Cortical thickness (cm)				
Median (IQR)	1.2 (1.0–1.4)	1.1 (1.0–1.3)	1.3 (0.9–1.6)	0.06

IQR: interquartile range,
[a] Cockroft-Gault formula,
[b] increased echogenicity.

4. Discussion

In this study, we examined the use of on-site smartphone microscope devices in the allograft renal biopsy procedure. In the analysis, we found that the use of a smartphone microscope retrieved more glomeruli and improved diagnostic yield compared to the standard procedure.

Table 3. Comparison of the pathological results between the smart lens and standard group.

	Smart lens group	Standard group	p-value
Number of tissue cores			
Mean (SD)	3.5 (0.7)	2.9 (0.9)	0.019*
Number of glomeruli			
Mean (SD)	8.3 (5.4)	7.1 (4.7)	0.72
Positive glomeruli, n (%)	43 (100)	39 (83)	0.005*
Inadequacy for diagnosis, n (%)	3 (7)	10 (21.3)	0.05*
Graft rejection, n (%)	29 (63)	27 (57.5)	0.61

SD: standard deviation, *Statistical significance.

The utility of on-site evaluation of the adequacy of kidney biopsy was studied and there are conflicting results. Gilani et al showed that the use of on-site dissecting of light microscopes resulted in more total glomeruli and adequate rate [8].

Sekulic et al, on the other hand, reported that the use of a dissecting microscope for on-site evaluation did not result in more glomeruli in the specimen [14]. Ferrer et al. also showed that the use of on-site evaluation did not improve the diagnostic yield in native kidney biopsy [7].

As for allograft kidney biopsies, Ferrer et al. reported that the use of on-site evaluation resulted in increased total glomeruli and a less inadequate rate for diagnosis [7]. This is also confirmed by the recent study by Wooldridge et al. which stated that the rate of inadequacies in allograft biopsied increased significantly when the tissue procurement method at the bedside was omitted [9].

The rate of the inadequacy of allograft specimens was 21.3% without on-site evaluation which is comparable to the rate reported by Wooldridge et al. of 21.6% [9]. However, the inadequacy rate was lower in our

study when the smartphone microscope was used by only 7% compared to 12.5% in the previous study [9].

Our study differs from the previous studies regarding the performing practitioner and the on-site evaluator [7, 8, 9]. All procedures in our study were exclusively performed by the urologists since it is the institutional protocol for allograft biopsy. Moreover, all specimens were also evaluated by the performing urologist, not the pathologist or the technician. This is believed to be the strength of this study since the one who evaluated the tissue was the one who was responsible for the procedure.

Even though Ferrer et al [7] showed that the procedure performed by radiologists was the predictor for a greater amount of cortex, it did not lead to increased diagnostic yield. In some centers, however, there is a trend toward the interventional radiologist to perform the percutaneous renal biopsy rather than nephrologist [15, 16].

Limitations in our study include small sample size, the heterogeneity of the experience of the surgeons in terms of evaluating the specimen, and a non-randomized method which could have led to selection bias due to the operator's preference. We did not include any of the native kidney biopsy or procedures done by nephrologists or radiologists. The adequacy of the specimen was defined using only the light microscope and there was no data regarding the use of immunofluorescence or electron microscope [17].

In conclusion, the use of on-site evaluation by the smartphone microscope significantly increased the number of glomeruli obtained and the diagnostic yield. It is inexpensive and convenient, especially for the resource-limiting center.

Declarations

Author contribution statement

Natthida Incharoen, Ukrit Rompsaithong, Pakorn Kiatsopit and Supanut Lumbiganon: Performed the experiments; Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data.

Wichien Sirithanaphol and Jarin Chindaprasirt: Conceived and designed the experiments; Performed the experiments; Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data; Wrote the paper.

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Data availability statement

Data will be made available on request.

Declaration of interests statement

The authors declare no conflict of interest.

Additional information

No additional information is available for this paper.

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