นิพนธ์ต้นฉบับ

Conventional renal biopsy in adult patients in Songklanagarind Hospital: analysis of bleeding and risk factors

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Abstract:

Conventional renal biopsy in adult patients in Songklanagarind Hospital: analysis of bleeding and risk factors

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Objective: *Although conventional renal biopsy is a useful procedure in determining renal histological diagnosis and guiding treatment, bleeding is a major complication even with experienced nephrologists. A new method of renal biopsy, the real-time ultrasound guided spring-loaded gun biopsy, has been developed. Some reports show less bleeding with this new method, but it is also more expensive. Bleeding in conventional renal biopsy in Songklanagarind Hospital has not been studied before. The purpose of this study was to find the extent of clinical bleeding of the conventional renal biopsy, to look at whether the new method of renal biopsy would be appropriate, and to identify the risk factors involved.*

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Design: *A retrospective study*

Patients: *Adult patients who underwent a kidney biopsy by medical nephrologists from January 1, 1992 to December 31, 1996 were included. Overall, 194 renal biopsies from 184 patients were analyzed.*

Methods: *Data were collected from medical records. Minor bleeding was defined as asymptomatic gross hematuria. Major bleeding was defined as bleeding that had clinical significance such as being associated with intense pain, needing a blood transfusion or requiring an intervention to stop the bleeding. A P-value less than 0.05 was considered to be statistically significant.*

Results: *Bleeding occurred in 13.4% of cases. Most were of a minor nature (88.8%). The major bleeding rate was 1.5%. These cases were gross hematurias that required blood transfusion and perirenal hematoma that had intense pain in 1% and 0.5% respectively. All stopped spontaneously and no cases needed intervention or died. There was a significantly lower hematocrit and number of total glomeruli in the bleeding group than in the no-bleeding group (28.9 ± 7.66 vs. 33.1 ± 8.5, p = 0.02 and 14.0 ± 11.1 vs. 20.3 ± 13.3, p = 0.02 respectively). Female patients tended to have a higher rate of bleeding than male patients (17% and 8% respectively, p = 0.062). Multivariate analysis indicated that an increase of every 1 total glomeruli decreased, and pre-biopsy hematocrit lower than 25% increased, the risk of bleeding (odds ratio 0.96 and 2.76 respectively).*

Conclusion: *There was a high bleeding rate, but most cases were minor. The major bleeding had a low clinical impact on patient morbidity and mortality. The associated factors were lower hematocrit and improper renal biopsy technique.*

Key words: *conventional renal biopsy, hematuria, bleeding*

บทคัดย่อ:

วัตถุประสงค์: *การเจาะไตมีประโยชน์มากในการวินิจฉัยพยาธิสภาพในไต ปัญหาแทรกซ้อนที่สำคัญคือ ภาวะเลือดออกหลังการเจาะไต มีการพัฒนาวิธีการเจาะเพื่อลดปัญหาแทรกซ้อนดังกล่าวแต่เครื่องมือมีราคาแพงกว่าการเจาะไตแบบมาตรฐานดั้งเดิม ยังไม่เคยมีการศึกษาอุบัติการณ์ของการมีเลือดออกหลังการเจาะไตโดยวิธีการเจาะไตแบบมาตรฐานดั้งเดิม การศึกษานี้เพื่อหาอุบัติการณ์และปัจจัยเสี่ยงของภาวะเลือดออกหลังการเจาะไตเพื่อเป็นประโยชน์ในการพิจารณาถึงความจำเป็นที่จะต้องเปลี่ยนวิธีการเจาะไต*

รูปแบบการศึกษา: *การศึกษาเชิงพรรณนาแบบย้อนหลัง*

ผู้ป่วย: *การเจาะไตทั้งหมด 194 ครั้ง จากผู้ป่วยผู้ใหญ่ 184 ราย*

วิธีการศึกษา: *เก็บข้อมูลต่าง ๆ จากเวชระเบียนผู้ป่วยใน การตกเลือดเล็กน้อย หมายถึง การมีปัสสาวะเป็นเลือดสด การตกเลือดรุนแรง หมายถึง การตกเลือดหรือปัสสาวะเป็นเลือดสดที่มีอาการปวดรุนแรงหรือต้องการเลือดทดแทนหรือใช้การสวนหลอดเลือดแดงในไตหรือการผ่าตัดเพื่อหยุดเลือด วิเคราะห์ข้อมูลด้วย SPSS for window V.9 แสดงข้อมูลด้วยจำนวนหรือร้อยละหรือค่าเฉลี่ย ± ค่าเบี่ยงเบนมาตรฐาน เปรียบเทียบความแตกต่างของข้อมูลระหว่างกลุ่มด้วย student t-test หรือ chi-square หรือ Kruskal-Wallis เมื่อเหมาะสม ทดสอบหาปัจจัยเสี่ยงอิสระด้วย multilple logistic regression analysis ค่า p น้อยกว่า 0.05 ถือว่ามีนัยสำคัญทางสถิติ*

ผลการศึกษา: *อัตราการเกิดเลือดออกหลังการเจาะไตคิดเป็นร้อยละ 13.4 ส่วนใหญ่ร้อยละ 88.8 เป็นการตกเลือดไม่รุนแรง มีเพียงปัสสาวะเป็นเลือดสดแล้วหยุดได้เอง การตกเลือดรุนแรงจนมีอาการปวดมากหรือต้องได้เลือดทดแทนมีเพียงร้อยละ 1.5 เท่านั้น การเจาะไตที่มีเลือดออกแทรกซ้อนมีระดับความเข้มข้นของเม็ดเลือดแดงและจำนวนโกลเมอรูไลน้อยกว่าการเจาะไตที่ไม่มีเลือดออกแทรกซ้อนอย่างมีนัยสำคัญทางสถิติ (28.9 ± 7.6 และ 33.1 ± 8.5 และ 14.0 ± 11.1 และ 20.3 ± 13.3, p = 0.02 ตามลำดับ) เพศหญิงมีแนวโน้มจะเกิดเลือดออกหลังเจาะไตสูงกว่าเพศชาย (ร้อยละ 17 และ 8 ตามลำดับ, p = 0.062) การวิเคราะห์ตัวแปรหลายตัวด้วย multiple logistic regression analysis พบว่าความเข้มข้นของเม็ดเลือดแดงที่น้อยกว่าร้อยละ 25 จะเพิ่มโอกาสเสี่ยงต่อการเกิดเลือดออกหลังการเจาะไตเป็น 2.76 เท่า และจำนวนโกลเมอรูไลเพิ่มขึ้น 1 ลูก จะลดโอกาสเสี่ยงต่อการเกิดเลือดออกหลังการเจาะไตเป็น 0.96 เท่า (p = 0.044 และ 0.028 ตามลำดับ)*

สรุป: *อุบัติการณ์ของภาวะเลือดออกหลังการเจาะไตที่แสดงอาการถือว่าสูง แต่ส่วนใหญ่เป็นภาวะเลือดออกระดับน้อย และมีผลกระทบต่อผู้ป่วยน้อยมาก ปัจจัยที่สัมพันธ์กับภาวะเลือดออกคือความเข้มข้นของเม็ดเลือดแดงต่ำ และวิธีการได้เนื้อไตที่ไม่เหมาะสม*

คำสำคัญ: *การเจาะไตแบบมาตรฐานดั้งเดิม, ภาวะตกเลือด, ปัสสาวะเป็นเลือด*

Introduction

Conventional renal biopsy is the most useful method for definite histological diagnosis of renal diseases, and is also helpful in guiding treatment. Bleeding which is related to gross hematuria and perirenal hematoma is the most common complication. Reported incidences of bleeding vary from 3.8 to 29%, depending on the definition of bleeding used, the methods of investigation, and needle size.[1-6]

New methods of renal biopsy, such as the real-time ultrasound-guided spring-loaded gun biopsy with a smaller needle, have been developed in an attempt to lessen the complications. Although retrospective comparative studies on this method have shown conflicting results[2-6], one prospective randomized comparative study demonstrated a lesser incidence and extent of perirenal hematoma.[7]

In Songklanagarind Hospital, the bleeding complications of conventional renal biopsy have never been studied. The present study aimed to analyze bleeding after a conventional renal biopsy to find out whether it would be of cost-benefit advantage to change to this new method of renal biopsy, which is more expensive (100-200 vs. 1,500-1,800 baht respectively). Risk factors of bleeding were also analyzed.

Materials and Methods

We retrospectively reviewed the results of conventional renal biopsies from 1 January 1992 to 31 December 1996. Included patients were over 14 years of age and had had a renal biopsy performed by medical nephrologists. The data were collected from the medical records and included age, sex, indication for renal biopsy, diastolic and systolic blood pressure, pre-biopsy hematocrit, coagulogram, number of glomeruli, histological diagnosis, severity of chronicity of renal histology, and complications of the renal biopsy.

In the biopsy procedure at Songklanagarind Hospital, the lower pole of the kidney is marked with an ultrasonogram, the skin is sterilized with betadine and anesthetic with 1-2% of xylocaine. The kidney lower pole is again confirmed by the movement of the spinal needle before a conventional Tru-Cut 14G needle renal biopsy is performed. After the procedure, the patient remains in bed for 12-18 hours. Vital signs and urine are observed and also symptoms of pain monitored.

Bleeding cases were separated into 2 groups. Minor bleeding was defined as gross hematuria. Major bleeding was bleeding that had clinical significance such as being associated with intense pain, needing a blood transfusion or requiring an intervention.

Histological diagnosis and chronicity of vascular and tubulointerstitial changes were reviewed by one pathologist. Total number of glomeruli was counted, vascular changes were defined as yes-no changes, while tubulointerstitial changes were semiquantitatively defined as no, mild, moderate or severe changes according to the degree of inflammation, interstitial fibrosis and tubular atrophy.

Statistical analysis was performed with SPSS for Windows v.9. Results were expressed as number with percentage or mean ± standard deviation. T-test was used to compare means for the quantitative data. Chi-Square and Kruskal-Wallis tests were used to compare the differences between groups for the qualitative data as appropriate. Results of multiple logistic regression included odds ratio and 95% confidence interval. $P<0.05$ was considered to be statistically significant.

Results

There were 218 procedures in the 208 cases of conventional renal biopsies during the study period. Twenty four procedures were excluded because medical records could not be retrieved, leaving data from 194 procedures to be analyzed. One hundred and nine renal biopsies were done on female patients (56%). The mean age of patients was 35.82 ± 15.03 years. The indications for a renal biopsy were steroid-resistant nephrotic syndrome in 33% (64 procedures), acute renal failure in 25.8% (50 procedures), chronic renal failure in 19.1% (37 procedures), steroid-dependent nephrotic syndrome in 9.3% (18 procedures), new case of nephrotic syndrome in 5.7% (11 procedures), relapse case of nephrotic syndrome in 3.6% (7 procedures), non-nephrotic range proteinuria in 1.5% (3 procedures), asymptomatic non-nephrotic range proteinuria and hematuria in 1.5% (3 procedures), and hematuria in 0.5% (1 procedure).

Overall there was clinical bleeding in 13.4% of procedures. Minor bleeding occurred in 23 procedures (11.9%), and major bleeding occurred in only 3 procedures (1.5%), in which there was intense pain from a perirenal hematoma and gross hematuria that needed blood transfusions in 1 and 2 procedures respectively. No case needed an intervention or died.

Ninty-one percent of biopsies were adequate for histological diagnosis when any non-global sclerotic glomeruli were obtained, but if at least 5 non-global sclerotic glomeruli was used as the tissue adequacy criterion[1], only 85% were adequate for histological diagnosis. The most common histological diagnoses from the renal biopsies were lupus nephritis in 34% (66 biopsies), mesangial proliferative glomerulonephritis in 15% (29 biopsies) and focal segmental glomerulosclerosis in 11% (21 biopsies), as shown in Table 1.

The basic data from the procedures with bleeding and without bleeding are shown in Table 2. Age, systolic and diastolic blood pressure, blood urea nitrogen, and creatinine were similar between groups. The bleeding group had a significantly lower hematocrit than the no-bleeding group (29% versus 33%, p = 0.02). The bleeding group also had a significantly lower number of glomeruli than the no-bleeding group (14 versus 20, p = 0.02).

Table 1 Histological diagnosis and bleeding

Histological diagnosis	Number of biopsies (percent)	Number of bleeding biopsies (percent)
Lupus nephritis	66 (34)	11 (16.7)
Mesangial proliferative GN	29 (15)	1 (3.4)
Focal segmental glomerulosclerosis	21 (11)	2 (9.5)
Membranous nephropathy	15 (8)	1 (6.7)
End-stage glomerular disease	12 (6)	1 (8.3)
Minimal change disease	8 (4)	1 (12.5)
Crescentic glomerulonephritis	5 (3)	0 (0)
Diabetic nephropathy	4 (2)	1 (25)
Chronic glomerulonephritis	4 (2)	0 (0)
Membranoproliferative glomerulonephritis	3 (1.5)	1 (33.3)
Goodpasture's syndrome	3 (1.5)	0 (0)
Interstitial nephritis	2 (1)	1 (50)
Amyloidosis	1 (0.5)	1 (100)
Graft rejection	1 (0.5)	1 (100)
Cryoglobulinemic glomerulonephritis	1 (0.5)	0 (0)
Thrombotic thrombocytopenic purpura	1 (0.5)	0 (0)
Inadequate	18 (9)	4 (22.2)

Table 2 Data comparing procedures with and without bleeding

Data	Procedures without bleeding (n = 168)	Procedures with bleeding (n=26)
Age (yrs)	36 ± 15	35 ± 13
Systolic BP (mmHg)	141 ± 22	143 ± 27
Diastolic BP (mmHg)	91 ± 14	92 ± 20
Hematocrit (%)	33 ± 8	29 ± 8*
BUN (mg%)	59 ± 43	70 ± 53
Creatinine (mg%)	5 ± 5	7 ± 9
Number of glomeruli (n)	20 ± 13	14 ± 11*

*p = 0.02

Table 3 Incidence of bleeding according to each putative risk factor

Factors	Clinical bleeding rate (cases/total)(%)*
Group of hematocrit	
> 30%	10/111 (9)
25-30%	6/29 (20)
< 25%	10/44 (22)
Sex	
Female	19/109 (17)
Male	7/85 (8)
History of hypertension	
yes	9/50 (18)
No	17/144 (12)
Indication of biopsy	
Acute renal failure	11/50 (22)
Chronic renal failure	5/37 (14)
New nephrotic syndrome	2/11 (18)
Others	8/96 (8)
Systolic BP (mmHg)	
</= 140	14/111 (13)
> 140	12/82 (15)
Diastolic BP (mmHg)	
</= 90	14/119 (12)
> 90	12/74 (16)
Vascular changes	
No	14/104 (13)
Yes	10/77 (13)
Tubulointerstitial changes	
No	5/28 (18)
Mild	6/70 (9)
Moderate	7/46 (15)
Severe	6/38 (16)

*The difference between groups in each parameter was not significant, p > 0.05, except hematocrit, which was significantly different between groups (p = 0.047).

Putative factors that may indicate a risk of bleeding are shown in Table 3. All patients had normal coagulation studies (data not shown). Histological diagnoses, as shown in Table 1, had an insignificant statistical connection with bleeding. The sex of patients, history of hypertension, normal systolic and diastolic blood pressure, indications for biopsy, chronicity of vascular and tubulointerstitial changes had similar clinical bleeding rates as shown in Table 3. However, female patients had a tendency to a higher rate of clinical bleeding (17% and 8%, p = 0.062). Procedures with inadequate tissue for histological diagnosis had a higher clinical bleeding rate than procedures with adequate tissue, but the difference did not reach statistical significance (22.2% and 12.5%, p > 0.05).

The results of the multiple logistic regression analysis are listed in Table 4. Total glomeruli and hematocrit lower than 30% are the two independent variables that predict the bleeding complication after conventional renal biopsy. Female sex also tended to be an independent associated factor.

Table 4 Odds ratio of significant variables

Variables	Odds ratio	95% confidence interval	P-value
Total glomeruli	0.96	0.92-0.99	0.028
Hematocrit			
> 30%	1.00		
25-30%	2.60	0.82-8.19	0.105
< 25%	2.76	1.02-7.41	0.044
Female	2.28	0.88-5.91	0.09

Discussion

Our study revealed a high clinical bleeding rate after conventional renal biopsy, but this was in a similar range to that of other studies.[2-6, 9] This may result from the experience level of the operators, kidney marking before biopsy, or the renal diseases per se. Another possible reason might be that less weight was given to contraindications to renal biopsy than in other studies[1], since we also performed renal biopsies in patients with blood pressure higher than 140/90 mmHg. However, most of the clinical bleeding was minor, and related to gross hematuria. This was similar to the study of Burstein, Korbet and Schwartz[5] and Marwah and Korbet[9], but differed from other studies[4, 7], which found perirenal hematoma. The reason could be different modes of investigation, as we did not routinely do ultrasonograms or computerized tomography postbiopsies. The major bleeding complication rate was similar to the other studies[1, 3, 4, 7], although lower than the study of Burstein, Korbet and Schwartz[5] and Marwah and Korbet[9], and it had a very small effect on patient morbidity. So, the change to the new technique of renal biopsy, which is more expensive, may not be justified on clinical grounds. This should be tested further by a prospective comparative study.

Although Parrish found that the bleeding rate was higher in procedures with unsatisfactory samples[1] and blood pressure higher than 140/90 mmHg[8], our study did not support these findings. Although the procedures with inadequate tissue had a higher rate of bleeding, this did not reach statistical significance. This may be the effect of a small sample size and a low incidence of clinical bleeding.

We found 2 independent associated risk factors. One was a lower pre-biopsy hematocrit in the bleeding group, similar to the study of Marwah and Korbet.[9] This may be explained by the poor interaction between platelets and endothelial cells[10] in an anemic state. So before a biopsy is performed, we suggest raising hemtocrit level to be 30%. The other was the lesser number of glomeruli in the specimens. This may imply that an improper technique was done, since some tissue samples had only a small cortex and some had only the medulla. We have no explanation for the female patients that tended to be association with bleeding. This should be confirmed by a larger prospective study.

Since this is a retrospective descriptive study, some data were missing and this may have affected the results from the tested risk factors. There were some factors that may be associated with risk, but they could not be analyzed, such as the experience of the ultrasonographers who located the lower pole of the kidney, the operating surgeons, and number of trials of the renal biopsy procedures.

Conclusion

We found a high rate of clinical bleeding following post-conventional renal biopsies, but most were minor. The major bleeding had a very low impact on patient morbidity. The associated factors were a low hematocrit and, possibly, improper biopsy technique.

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