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## Publication Ethics

Publication ethics of Greater Mekong Subregion Medical Journal (GMSMJ)

Greater Mekong Subregion Medical Journal presents articles in the field of basic and advanced clinical research in medicine and related health sciences, medical education as well as community medicine in Thailand and international, especially in countries of Greater Mekong Subregion.

The journal publishes 3 issues a year: Issue 1 (January - April), Issue 2 (May - August) and Issue 3 (September -December). All submitted research articles and review articles will be evaluated by a single blinded peer-review process and reviewed by 2 experts who have knowledge, expertise, and experience in the field of medicine and related health sciences prior to publication. The journal encloses the information of authors and reviewers. In case of a difference of evaluation, the article evaluation will be considered and given a final decision.

Greater Mekong Subregion Medical Journal establishes the roles and duties for three different groups in the process of article publication: author (s), editor, and reviewers. The following information is given to the three groups of people so that they will strictly abide by its benefits of those concerns, including readers and others in academia.

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Original Article

GMSMJ

Greater Mekong Subregion Medical Journal

# Computer-based Renal Sonographic Image Analysis of Renal Progression among Patients with Chronic Glomerulopathies

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## Abstract:

**Background:** Renal sonography is a useful diagnostic imaging procedure already used in chronic glomerulopathies (CGN). Quantitative renal echogenicity has not been formerly evaluated in regard to its capacity to identify patients at risk for progressive renal disease.

**Objective:** The study aimed to predict renal progression using computer-based image analysis of renal sonographic findings and to explore association between renal sonographic findings and renal histopathologic indices.

**Method:** Renal sonography was performed on 37 patients with CGN undergoing renal biopsy. Sonographic images were processed and analyzed using computer programs to determine quantitative renal cortical echogenicity. Patients were followed up over a 3-month period to evaluate renal progression correlated with estimated glomerular filtration rate (GFR).

**Results:** Among patients with CGN undergoing renal biopsy, total renal cortical echogenicity and long axis echogenicity were significantly higher in those patients with renal progression. Using multivariable analysis, high renal echogenicity showed significant association with increased risk of worsening renal function among patients with CGN (HR 1.13, 95%CI 1.01-1.25). Long axis renal echogenicity (AUC 0.71; 95%CI 0.52-0.89), combined with other findings (AUC 0.93; 95%CI 0.84-1.00) achieved a better score predicting CKD progression in the CGN group. Furthermore, renal to liver echogenicity ratio correlated significantly to interstitial fibrosis and tubular atrophy. Renal/liver echogenicity ratio (AUC 0.83; 95%CI 0.69 to 0.97), combined with other findings (AUC 0.95; 95%CI 0.88 to 1.00), achieved a perfect score predicting IFTA > 50% in the CGN group.

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**Conclusion:** Quantitative renal cortical echogenicity using computer-based image analysis might be a useful tool to identify patients with CGN and renal progression related to renal fibrosis.

**Keywords:** Renal ultrasound, Computer-based image analysis, CKD progression

## Introduction

Renal sonography is a reliable and noninvasive diagnostic tool, providing ease of use and valuable information concerning structural changes, especially among patients with chronic kidney disease (CKD).[1] Decreased kidney length, cortical parenchymal thickness and increased parenchymal echogenicity could represent CKD parenchymal damage.[2] Renal sonographic information can assess CKD status, and significant correlation was found between cortical thickness, renal length and estimated glomerular filtration rate (eGFR).[3,4]

Several studies have demonstrated association of sonographic findings with renal histopathologic findings. Initial investigation indicated that renal cortical echogenicity correlated to severity of global sclerosis, tubular atrophy, the number of hyaline casts per glomerulus and focal leukocytic infiltration.[5] One later study, revealed significant correlation between the degree of cortical echogenicity and glomerulosclerosis or tubular atrophy, but without any correlation to interstitial fibrosis.[6] Recently another study confirmed that renal length and cortical thickness predicted renal progression and histopathologic changes, especially, after weighting for cortical echogenicity, when scored by comparison with liver echogenicity.[7]

The reliability of renal sonography is questionable because sonographic dimensions and quantitative measurement are often operator dependent. The use of computer-assisted image analysis has become increasingly accessible in many areas and has also provided greater accuracy in the interpretation of various types of image studies. One recent study indicated that using a comprehensive approach to analyze and classify CKD stages, according to renal sonographic images, when assisted by an image-processing model, identified potential patients with CKD at early stages.[8] However, data about the relationship between renal progression and renal sonographic assessment, using computer-assisted image analysis, among patients with chronic glomerulopathy (CGN) are limited. In this study, we aimed to predict renal progression using computer-based image analysis of renal sonographic findings. We also aimed to investigate association between renal sonographic findings and chronic histopathologic findings.

## Methods

### Study design

This study employed a prospective cohort design (diagnostic test), conducted on enrolled patients with CGN, attending Phramongkutklao Hospital, during June through to November 2021. The trial was approved by the Ethics Committee of the Institute Review Board at the Royal Thai Army Medical Department (IRBRTA) April 28, 2021, with code R037h/64. This study was registered with Thai Clinical Trials code TCTR202203211001.

### Study population

The inclusion criteria comprised patients aged over 18 years with CGN, who were undergoing renal biopsies and could provide informed consent. Patients with obstructive uropathy, renal tumor, single kidney, polycystic kidney disease, transplanted kidney, pregnancy, body mass index more than 30 kg/m$^2$ and end stage kidney disease were excluded.

**Laboratory measurements**

Biochemical parameters and albuminuria were measured in serum and urine using a Roche P800 Modular Chemistry Analyzer (Roche Diagnostics, Basel, Switzerland), measurement being performed at baseline and after three months. The eGFR was estimated from serum creatinine using the CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration) formula[9] and CKD progression was defined as an eGFR-CKD-EPI decline of more than 25% from baseline within one year.

**Renal ultrasonography**

Ultrasonographic studies on kidneys were carried out using a Philips HD3-EXP ultrasound machine with 3.5 MHz convex transducer. Renal sonography was performed by a single nephrologist with 10 years of experience in the field of renal sonography in the outpatient department of our renal unit and the investigator was blinded regarding patients' histories and laboratory results. Renal sonographic parameters including kidney length, parenchymal thickness and parenchymal echogenicity were obtained from both kidneys. The renal sonographic images were captured in both longitudinal and short axis views, 8 to 10 images each. Renal images were collected and compared with liver images, comprising 2 to 5 images for each patient, for renal to liver echogenicity ratio measurement. All pictures were obtained in a .jpg file and all ultrasound images were performed by a single nephrologist.

**Computer assisted image analysis**

Sonographic images were analyzed by the department of Computer Science, Faculty of Science, Kasetsart University and were similar to previously used protocols.[8] At the beginning, the systems required users to define the area of interest, focusing on three main areas: the cortical area, calyceal system and whole renal contour. To ensure the precise definitions of the renal contours using an ultrasound image, the boundaries between different parts of the kidney were initially identified in polygonal points, using a LabelMe Program. After that, polygonal masking was performed, by coding in a MATLAB Program, to differentiate renal cortex areas from any renal cyst and calyceal areas (Figure 1).

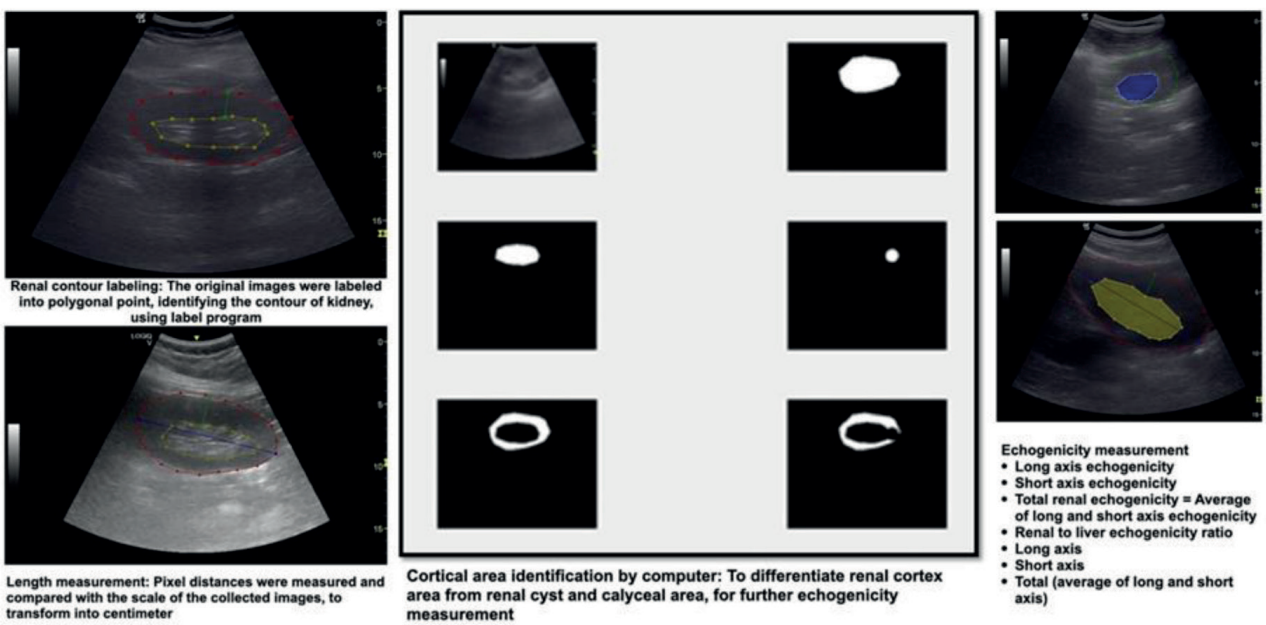



**Figure 1** Analysis of sonographic images

The next step was cortical echogenicity measurement. Sonographic images were transformed to small discrete elements called pixels and echogenicity measurements were demonstrated in numerical value, representing the intensity of a particular channel at the location of a pixel. In each patient, renal echogenicity was measured, to obtain an average value, within the sets of pictures. These were classified by the captured view as follows. Long axis echogenicity, short axis echogenicity, total renal echogenicity, which is the average of long and short axis echogenicity and finally the renal to liver echogenicity ratio, which is renal echogenicity compared with liver echogenicity. Length was measured using the longest pixel distances compared with the scale of the collected images, converted to centimeters. Furthermore, deep learning model training to identify renal contour was performed, using YOLO v5 training model (Figure 1).

In those patients with CGN, admitted for renal biopsy, the histopathologic grading of chronic changes in native renal biopsy samples were evaluated by a single renal pathologist, focusing on glomerulosclerosis, interstitial fibrosis and tubular atrophy (IFTA), using a modified NIH lupus nephritis activity and chronicity scoring system.[10]

**Statistical analysis**

The results were expressed as mean ± standard deviations or as median with interquartile range (IQR) according to data distribution. Difference between groups was analyzed using Chi-square, Mann–Whitney U and Student's t tests. Univariate analysis was performed to explore relationships between renal progression and renal histologic findings and other ultrasonographic variables, employing a Pearson correlation test for normally distributed data and a Spearman Rank correlation test for nonparametric data. We also conducted multivariate analysis for CKD progression prediction. Results underwent characteristic (ROC) analysis and the areas under the curves (AUCs) were estimated to investigate the role of each renal sonographic parameter to determine CKD progression or renal fibrosis. Statistical significance was defined as P-value < 0.05.

**Results**

A total of 37 patients with CGN, 12 males and 25 females, were enrolled. Their mean age was 42.6 ± 13.2 years. As shown in Table 1, baseline characteristics of patients with CKD progression and no CKD progression did not differ. As recorded, 6 (16.2%) patients presented with diabetes mellitus, and 16 (43.2%) patients had lupus nephritis. The correlation of long axis echogenicity, systolic blood pressure, baseline estimated GFR, and urine albumin to creatinine ratio (UACR), to GFR progression, among patients with CGN undergoing renal biopsy is illustrated in Figure 2.

**Renal sonography and CKD progression**

Total renal echogenicity (50.59 ± 10.33 vs. 43.61 ± 9.45, P = 0.049) and long axis echogenicity (50.18 ± 11.58 vs. 41.91 ± 8.62, P = 0.02), were significantly higher among patients with CKD progression in the CGN group (Table 2). Multivariate analysis was performed to determine their relative contributions to echogenicity. When adjusted for underlying diabetes mellitus, prednisolone use and baseline UACR, renal progression showed significant independent contributions to both total renal echogenicity (adjusted HR 1.13, 95% CI, 1.01 to 1.25) and long axis echogenicity (adjusted HR 1.14, 95%CI, 1.02 to 1.29) (Table 3).

**Table 1** Baseline characteristics

| Variable | CKD progression (N=12) | Non-CKD progression (N=25) | P-value |
|---|---|---|---|
| Male (%) | 25 | 40 | 0.371 |
| Age (year) | 42.1 ± 12.1 | 43.4 ± 14.5 | 0.781 |
| BMI (kg/m$^2$) | 24.3 ± 5.3 | 24.7 ± 5.1 | 0.807 |
| Underlying diseases N (%) | | | |
| • Type 2 diabetes | 4 (33.3) | 2 (8) | 0.050 |
| • Hypertension | 4 (33.3) | 7 (28) | 0.740 |
| • Lupus nephritis | 4 (33.3) | 12 (48) | 0.399 |
| Medications N (%) | | | |
| • Prednisolone | 7 (58.3) | 21 (84) | 0.088 |
| • Other immunosuppressive agents | 5 (41.7) | 15 (60) | 0.295 |
| • ACEs/ARBs | 7 (58.3) | 20 (80) | 0.165 |

*UACR; Urine albumin to creatinine ratio, SBP; systolic blood pressure, DBP; diastolic blood pressure, eGFR; estimated glomerular filtration rate; ACEs; Angiotensin converting enzyme inhibitors, ARBs; Angiotensin receptor blockers.*

**Table 2** Computer-based sonographic findings in CGN biopsies

| Sonographic findings | CKD progression (N=12) | Non-CKD progression (N=25) | P-value |
|---|---|---|---|
| Total renal echogenicity | 50.59 ± 10.33 | 43.61 ± 9.45 | 0.049 |
| Total renal/liver echogenicity ratio | 1.24 ± 0.25 | 1.13 ± 0.24 | 0.238 |
| Long axis echogenicity | 50.18 ± 11.58 | 41.91 ± 8.62 | 0.020 |
| Long axis renal/liver echogenicity ratio | 1.22 ± 0.25 | 1.09 ± 0.23 | 0.117 |
| Short axis echogenicity | 51.36 ± 9.69 | 45.84 ± 10.70 | 0.140 |
| Short axis renal/liver echogenicity ratio | 1.26 ± 0.26 | 1.19 ± 0.27 | 0.452 |
| Cortical thickness (cm) | 1.78 ± 0.36 | 1.75 ± 0.30 | 0.788 |
| Renal length (cm) | 10.39 ± 0.35 | 11.06 ± 0.30 | 0.083 |

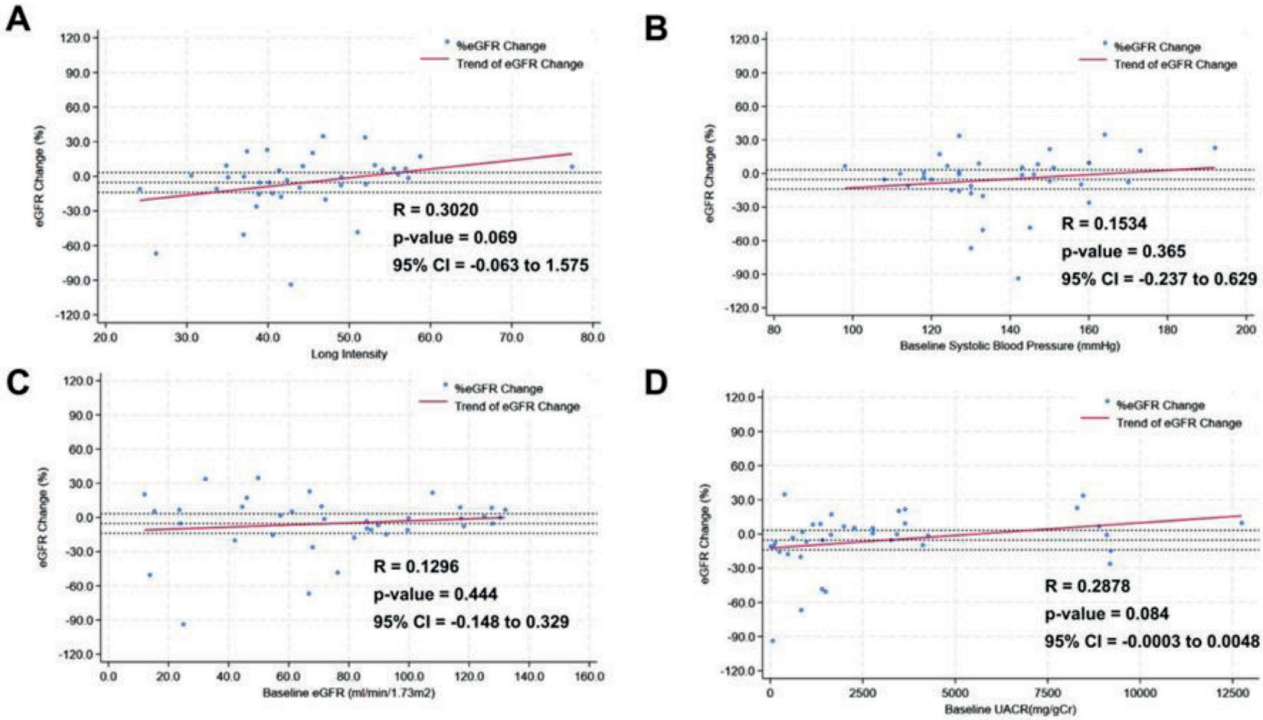



**Figure 2** Correlation of long axis echogenicity, systolic blood pressure, baseline estimated GFR and urine albumin creatinine ratio with GFR progression among patients with CGN undergoing renal biopsy

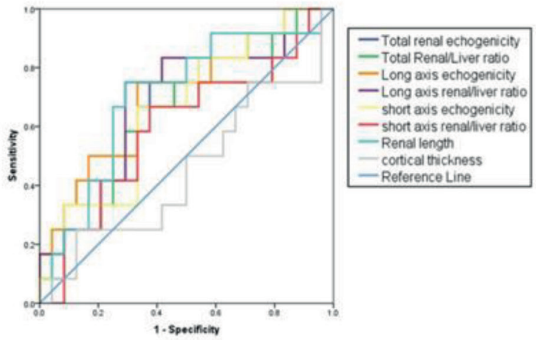
**Table 3** Multivariate analysis to predict CKD progression among patients with CGN undergoing renal biopsy

| | Unadjusted HR | 95% CI | P-value | Adjusted HR | 95% CI | P-value |
|---|---|---|---|---|---|---|
| Model 1 | | | | | | |
| Total renal echogenicity | 1.08 | (0.99, 1.17) | 0.060 | 1.13 | (1.01, 1.25) | 0.026 |
| Type 2 diabetes | 5.75 | (0.88, 37.62) | 0.068 | 8.11 | (0.65, 100.9) | 0.104 |
| Prednisolone | 0.27 | (0.56,1.28) | 0.099 | 0.30 | (0.40, 2.31) | 0.250 |
| UACR | 1 | (1.00,1.00) | 0.075 | 1.00 | (1.00,1.00) | 0.230 |
| Model 2 | | | | | | |
| Long axis echogenicity | 1.10 | (1.01, 1.20) | 0.037 | 1.14 | (1.02, 1.29) | 0.026 |
| Type 2 diabetes | 5.75 | (0.88, 37.62) | 0.068 | 8.83 | (0.65, 100.9) | 0.098 |
| Prednisolone | 0.27 | (0.56,1.28) | 0.099 | 0.33 | (0.40, 2.31) | 0.295 |
| UACR | 1 | (1.00,1.00) | 0.075 | 1.00 | (1.00,1.00) | 0.265 |

*UACR; Urine albumin to creatinine ratio, HR; Hazard ratio, Adjusted; T2DM, prednisolone and baseline UACR.*

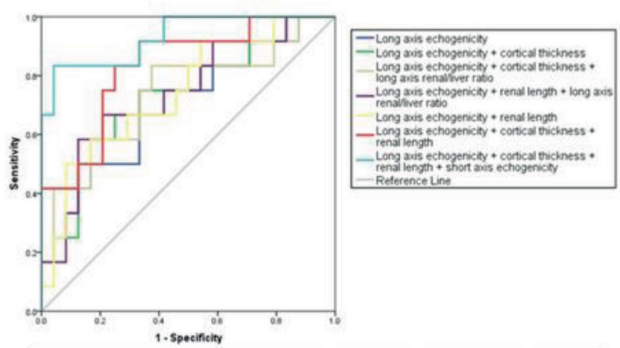
ROC analysis was performed to identify the best ultrasonographic parameters able to discriminate CKD progression from non-CKD progression in the CGN group. Long axis echogenicity was the only sonographic parameter that significantly predicted renal progression (AUC 0.71; 95% CI, 0.52 to 0.89) and when combined with other sonographic findings, including cortical thickness, renal length and short axis echogenicity, was able to achieve a better score to predict CKD progression in the CGN group (AUC 0.93; 95% CI, 0.84 to 1.00) (Figure 3).

**A. Area under the curve of predictive factors for CKD progression**




| Sonographic findings | AUC | 95% CI | *p*-value |
|---|---|---|---|
| Cortical thickness (cm) | 0.451 | (0.24, 0.61) | 0.638 |
| short axis renal/liver echogenicity ratio | 0.597 | (0.39, 0.80) | 0.347 |
| Total renal/liver echogenicity ratio | 0.635 | (0.44, 0.83) | 0.191 |
| Short axis echogenicity | 0.653 | (0.47, 0.84) | 0.140 |
| Total renal echogenicity | 0.681 | (0.49, 0.87) | 0.081 |
| Long axis renal/liver echogenicity ratio | 0.687 | (0.49, 0.88) | 0.070 |
| Renal length (cm) | 0.701 | (0.52,0.89) | 0.052 |
| Long axis echogenicity | 0.705 | (0.52, 0.89) | 0.048 |

**B. Area under the curve of long axis echogenicity combined with other parameters for CKD progression**




| Sonographic findings | AUC | 95% CI | *p*-value |
|---|---|---|---|
| Long axis echogenicity | 0.705 | (0.52, 0.89) | 0.048 |
| Long axis echogenicity + cortical thickness | 0.726 | (0.54, 0.91) | 0.029 |
| Long axis echogenicity + cortical thickness + long axis renal/liver ratio | 0.736 | (0.55, 0.92) | 0.022 |
| Long axis echogenicity + renal length + long axis renal/liver ratio | 0.740 | (0.56, 0.92) | 0.021 |
| Long axis echogenicity + renal length | 0.743 | (0.57, 0.92) | 0.019 |
| Long axis echogenicity + cortical thickness + renal length | 0.830 | (0.69, 0.97) | 0.001 |
| Long axis echogenicity + cortical thickness + renal length | 0.931 | (0.84,1.00) | < 0.001 |

**Figure 3** Area under the curve of predictive factors for CKD progression

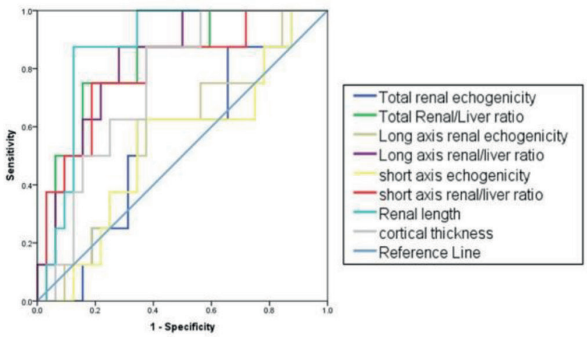
## Renal sonography and histopathologic findings

The median percentage of glomerulosclerosis was 31.67% (IQR 8.71 to 57.29), median of percentage of IFTA was 20% (IQR 5 to 40) and median of chronicity score was 4.5 (IQR 2.5 to 7.0). Percentage of IFTA positively correlated to total renal to liver echogenicity ratio (R = 0.399, P = 0.014), long and short renal to liver echogenicity ratio (R = 0.36, P = 0.023), short axis renal/liver echogenicity ratio (R = 0.40, P = 0.011) and negatively correlated to cortical thickness (R = -0.39, P = 0.013) and kidney length (R = -0.50, P= 0.001). The percentage of glomerulosclerosis and chronicity scores also negatively correlated with cortical thickness and renal length (Table 4).

ROC analysis of ultrasonographic parameters used to determine IFTA >50% among patients with CGN is illustrated in Figure 4. AUC to diagnose IFTA > 50% using kidney length, long axis renal to liver echogenicity ratio, total renal/liver echogenicity ratio, short axis renal/liver echogenicity ratio and cortical thickness were 0.87 (95% CI, 0.76 to 0.98), 0.83 (95% CI, 0.67 to 0.98), 0.82 (95% CI, 0.67 to 0.98), 0.79 (95% CI, 0.62 to 0.97) and 0.75 (95% CI, 0.59 to 0.91), respectively. The optimal long axis renal to liver echogenicity ratio was determined as 1.138 with a sensitivity of 87.5% and specificity of

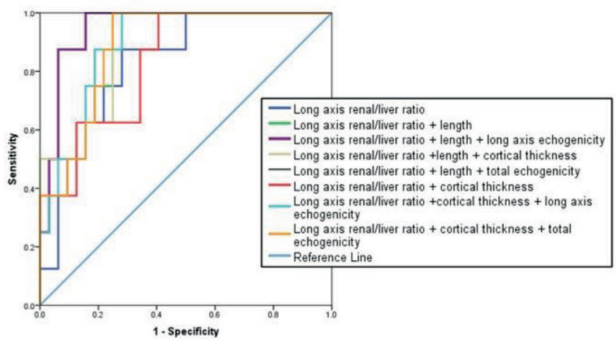
71.9% (AUC, 0.83; 95% CI, 0.67 to 0.98). The cutoff levels of long axis renal to liver echogenicity ratio, used to indicate IFTA > 50%, are also demonstrated in Table 5. In addition, combined long axis renal to liver echogenicity ratio with kidney length and long axis echogenicity achieved a perfect score predicting IFTA > 50% in the CGN group such as (AUC 0.95; 95% CI, 0.88 to 1.00).

**A. Area under the curve of predictive factors for IFTA>50%**




| Sonographic findings | AUC | 95% CI | *p*-value |
|---|---|---|---|
| Short axis echogenicity | 0.539 | (0.32, 0.76) | 0.735 |
| Total renal echogenicity | 0.563 | (0.36, 0.77) | 0.589 |
| Long axis echogenicity | 0.570 | (0.36, 0.78) | 0.543 |
| Cortical thickness (cm) | 0.746 | (0.59, 0.91) | 0.033 |
| short axis renal/liver echogenicity ratio | 0.793 | (0.62, 0.97) | 0.011 |
| Total renal/liver echogenicity ratio | 0.820 | (0.67, 0.98) | 0.006 |
| Long axis renal/liver echogenicity ratio | 0.828 | (0.69, 0.97) | 0.005 |
| Renal length (cm) | 0.871 | (0.76,0.98) | 0.001 |

**B. Area under the curve of Long axis renal/liver echogenicity ratio combined with other parameters for IFTA > 50%**




| Sonographic findings | AUC | 95% CI | *p*-value |
|---|---|---|---|
| Long axis renal/liver echogenicity ratio | 0.828 | (0.69, 0.97) | 0.005 |
| Long axis renal/liver ratio + cortical thickness | 0.887 | (0.78, 0.99) | 0.001 |
| Long axis renal/liver ratio + length + cortical thickness | 0.891 | (0.78, 0.99) | 0.001 |
| Long axis renal/liver ratio + cortical thickness | 0.891 | (0.79, 0.99) | 0.001 |
| Long axis renal/liver ratio + length | 0.895 | (0.79, 0.99) | 0.001 |
| Long axis renal/liver ratio + length + total echogenicity | 0.941 | (0.87,1.00) | < 0.001 |
| Long axis renal/liver ratio + length + long axis echogenicity | 0.949 | (0.88, 1.00) | < 0.001 |

**Figure 4** Area under the curve to determine IFTA > 50%

**Table 4** Correlation between sonographic findings and renal pathology

| Sonographic findings | Glomerulosclerosis (%) | IFTA (%) | Chronicity score |
|---|---|---|---|
| Total renal echogenicity | 0.16<br>P = 0.324 | 0.02<br>P = 0.918 | -0.05<br>P = 0.738 |
| Total renal/liver echogenicity ratio | 0.31<br>P = 0.055 | 0.39<br>P = 0.014 | 0.30<br>P = 0.065 |
| Long axis echogenicity | 0.13<br>P = 0.420 | -0.01<br>P = 0.953 | -0.09<br>P = 0.599 |
| Long axis renal/liver echogenicity ratio | 0.29<br>P = 0.072 | 0.36<br>P = 0.023 | 0.26<br>P = 0.102 |
| Short axis echogenicity | 0.17<br>P = 0.308 | 0.04<br>P = 0.830 | -0.03<br>P = 0.838 |
| Short axis renal/liver echogenicity ratio | 0.30<br>P = 0.059 | 0.40<br>P = 0.011 | 0.31<br>P = 0.053 |
| Cortical thickness (cm) | -0.51<br>P = 0.001 | -0.39<br>P = 0.013 | -0.41<br>P = 0.009 |
| Renal length (cm) | -0.45<br>P = 0.004 | -0.50<br>P = 0.001 | -0.47<br>P = 0.002 |

**Table 5** Cutoff value of long axis renal/liver echogenicity ratio to predict IFTA > 50%

| Long axis renal/liver echogenicity ratio | Sensitivity | Specificity | PPV | NPV | + LR | - LR |
|---|---|---|---|---|---|---|
| 1.102 | 87.5 % | 56.3 % | 33.33 | 94.74 | 2.00 | 0.22 |
| 1.123 | 87.5 % | 68.8 % | 41.18 | 95.65 | 2.80 | 0.18 |
| 1.138 | 87.5 % | 71.9 % | 43.75 | 98.83 | 3.11 | 0.17 |
| 1.157 | 75.0 % | 71.9 % | 40.00 | 92.00 | 2.67 | 0.33 |
| 1.189 | 62.5 % | 78.1 % | 41.67 | 89.29 | 2.89 | 0.48 |
| 1.239 | 62.5 % | 84.4 % | 50.00 | 90.00 | 4.00 | 0.44 |
| 1.353 | 50.0 % | 90.6 % | 57.14 | 87.88 | 5.33 | 0.55 |

## Discussion

In this study, we indicated that ultrasonographic parameters, including kidney length, parenchymal thickness and quantitative renal echogenicity, using computer-based image analysis, were associated with renal progression and fibrosis in renal histopathology among patients with CGN. Using computer-based image analysis, we defined new ultrasonographic parameters, such as long axis echogenicity, that significantly correlated to renal progression, as well as long axis renal to liver echogenicity ratios that correlated to the degree of renal fibrosis. Also, ROC curve analysis, to determine IFTA > 50%, showed that combining the long axis renal to liver echogenicity ratio with kidney length and long axis echogenicity, provided the best parameter, exhibiting the highest AUC.

Renal sonography is a useful diagnostic tool for kidney diseases, but the results of the test mainly depend on the physician's experience and can vary among operators. Thus, data about the best ultrasonographic parameters in evaluating CKD remain conflicting. We established a model of an image-processing system to evaluate and measure sets of renal images among patients with CGN to provide a more precise, accurate and reliable detection system.

Regarding the process of image analysis, we focused mainly on the measurement of echogenicity. Because of the lack of standardized measuring methods or cutoff value of the cortical echogenicity, many studies only visually evaluated this component, by comparing it with liver echogenicity and translating the results only to scaling scores and not by direct measurement. Several studies showed association between renal function and ultrasonographic parameters, including kidney length, parenchymal thickness and renal parenchymal echogenicity.[11,12] Our study notably found that both total renal echogenicity and long axis echogenicity predicted renal progression, and the combination of long axis echogenicity along with other sonographic findings achieved better parameters for the prediction of renal progression in patients with CGN.

Tubulointerstitial changes have been proven to better predict renal progression and prognosis in patients with CGN and diabetic nephropathy.[13] Based on the assumption that evidence of chronicity change would be a useful to guide therapy in CGN, a sonographic test, that is able to avoid unnecessary renal biopsies in severe CGN, would be a desirable diagnostic tool. One study showed that cortical renal echogenicity was related to tubular atrophy and interstitial inflammation.[6]

However, the level of renal parenchymal echogenicity is a subjective assessment. Our study found that renal echogenicity, augmented by computer based-imaging analysis, correlated well to tubulo-interstitial fibrosis, predicting irreversible impairment of renal function. Moreover, we confirmed that renal echogenicity levels, especially combined with other parameters, improved scoring for prediction of IFTA > 50% in the CGN group. For long axis renal to liver echogenicity ratio, the cutoff value 1.138 provided a sensitivity 87.5%, specificity 71.9%, negative predictive value 98.8% and likelihood ratio 0.17, which again could be helpful in predicting severe chronic change and therefore further refine the decision-making process for renal biopsy indication. Similar to related studies, quantitative renal echogenicity by kidney/liver ratio strongly determined irreversible kidney injury by renal histopathology score[14] and has also been shown to reflect the severity of damage in pediatric renal cases.[15]

Several limitations were encountered in this study. Firstly, this was a single-center referral care center study. Secondly, the number of patients was relatively few with a relatively short time to evaluate CKD progression. Thirdly, the study still requires internal and external validity to confirm its applicability because the renal ultrasonographic data was collected by a single nephrologist. However, the strength of our computer-based image analysis was that it required less time for quantitative echogenicity measurement, for example it only took 10 minutes for the analysis of 1,400 images, of great use in analysis of large data sets in future clinical trials.

## Conclusion

Quantitative renal cortical echogenicity, using computer-based image analysis, might be a useful tool to identify patients with CGN at risk of renal progression. Renal cortical echogenicity and thickness exhibited a close relationship to the degree of chronic tubulointerstitial changes among patients with CGN, who were referred for renal biopsy. The ultrasonographic parameters, using computer-based image analysis defined in this study, could provide more objective data in assessing CKD.[16] However, further large-scale clinical and research studies in CKD populations are needed to confirm our study results.

## Conflicts of interest

All authors have no conflict of interest to declare.

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This study did not receive any funding in any form.

## Data sharing statement

The data presented in this study are available on request from the corresponding author.

## Authors' contribution

Conceptualization: NC, AC, NN, PT, NV, PT, PI, WK, OS, BS

Data curation: NC, AC, NN, PT, OS

Formal analysis: NC, BS, OS

Methodology: NC, AC, BS

Project administration: NC

Writing-original draft: NC, AC, BS

Writing-review & editing: NC, AC, NN, PT, NV, PT, PI, WK, OS, BS

All authors read and approved the final manuscript.

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org/education/kidneyweek/2022/ program abstract. aspx? Control Id=3767577

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# Laparoscopic Cholecystectomy with Extracorporeal Sliding Knot using Knot Pusher: A Retrospective Study at Mae Fah Luang University Medical Center Hospital

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**Abstract:**

**Background:** The cystic duct and vessels ligation are critical step in laparoscopic cholecystectomy. Various techniques, including clips and knot-tying methods, have been developed to enhance the safety and efficacy of this ligation process.

**Objective:** This retrospective study endeavors to meticulously examine the efficacy of laparoscopic cholecystectomy performed using the extracorporeal sliding knot technique facilitated by a knot pusher in patients presenting with symptomatic gallstone diseases.

**Method:** A retrospective analysis of electronic medical records was conducted for cases of laparoscopic cholecystectomy (LC) performed using the extracorporeal sliding knot technique using knot pusher at Mae Fah Luang University Medical Center Hospital between July 2020 and July 2023. Data on patient demographics, surgical time, hospital stay, and postoperative complications were extracted and analyzed.

**Results:** The study revealed 118 patients, 29 were male (24.6%) and 89 were female (75.4%). The median age was 55.2 years, with a range of 23 to 85 years. The average surgical time was 20 minutes, with a range of 15 to 55 minutes. The average blood loss was 16 mL, with a range of 5 to 120 mL. The average hospital stay was 1.5 days, ranging from 1 to 4 days. Consist with 35% of co-medical diseases which hypertension the most common. No surgical complications were observed in any of the cases.

**Conclusion:** Laparoscopic cholecystectomy with the extracorporeal sliding knot technique offers an efficient and safe alternative for cystic duct and vessel ligation during gallbladder surgery.

**Keywords:** Laparoscopic cholecystectomy, Extracorporeal sliding knot technique, Knot pusher

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## Introduction

Laparoscopic cholecystectomy has become the preferred approach for managing gallbladder diseases due to its numerous advantages over open surgery. Cystic duct leakage is reported in 0.5 - 3% of patients following LC.[1,2] The safe ligation of the cystic duct and vessels is a critical step in this procedure.[3-5] Various techniques, including clips, knot-tying and vessel sealing devices, have been developed to enhance the safety and efficacy of this ligation process.[6,7] This study focuses on evaluating the effectiveness and safety of the extracorporeal sliding knot technique in LC.

## Method

A retrospective analysis of electronic medical records was conducted for 118 cases of LC performed using the extracorporeal sliding knot technique at Mae Fah Luang University Medical Center Hospital between July 2020 and July 2023. Data on patient demographics, surgical time, hospital stay, and postoperative complications were extracted and analyzed.

## Results

This retrospective study evaluated the outcomes of LC with extracorporeal sliding knot using knot pusher technique at Mae Fah Luang University Medical Center Hospital from July 2020 to July 2023. The study revealed the excellent outcomes for LC using knot pusher. Of the 118 patients, 29 were male (24.6%) and 89 were female (75.4%) as in Table 1. The median age was 55.2 years, with a range of 23 to 85 years. The average surgical time was 20 minutes, with a range of 15 to 55 minutes as in Table 2. The average blood loss was 16 mL, with a range of 5 to 120 mL. The average hospital stay was 1.5 days, ranging from 1 to 4 days. The co-medical diseases were 35% of the population studied. They consisted with hypertension, diabetes, COPD (Chronic obstructive pulmonary disease), CKD (Chronic kidney disease), and BPH (Benign prostatic hyperplasia). No surgical complications were observed in any of the cases. Among the cases, 32 were One Day Surgery (ODS) cases, and no surgical complications were observed.

## Subgroup Analysis: One Day Surgery

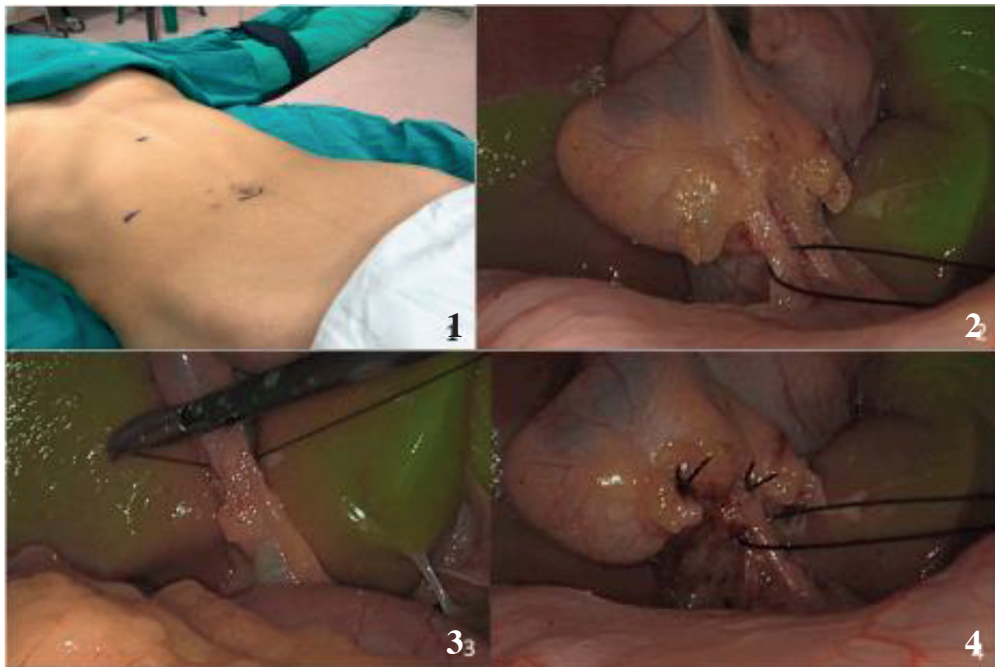
Among the 118 cases, 32 patients presented One Day Surgery (ODS). The surgical outcomes for this subgroup were consistent with those of the overall cohort, with no observed complications.

**Table 1** Demographic Data

| Demographics | N (%) |
|---|---|
| Gender | |
| Male | 29 (24.6) |
| Female | 89 (75.4) |
| Age | Mean 55.2<br>Range 23-85 |
| Co-morbidity | 41 (35.7%) |
| Hypertension | 35 (29.6%) |
| Diabetes | 24 (20.3%) |
| COPD | 18 (15.6%) |
| CKD | 12 (10.1%) |
| BPH | 5 (4.2%) |
| Previous abdominal surgery | 5 |
| Midline | 3 |
| Lateral | 2 |

**Table 2** Clinical Data

| | |
|---|---|
| Operation time | Mean 20 min<br>(Range 15-55) |
| Blood loss | Mean 16 mL<br>(Range 5-120) |
| Hospital stay | Mean 1.5 day<br>(Range 1-4) |
| One Day Surgery | 32 cases (27.1%) |




Highlight the Steps of Procedure

**Figure 1** Three ports; 10 mm. 2 × 5 mm, all ports site were infiltrated with local anesthesia
**Figure 2** Identify critical view of safety
**Figure 3** The cystic duct and vessels were loop with Nylon No.2
**Figure 4** A sliding knot was tied extracorporeally, then push inside abdominal cavity with my designed Knot Pusher

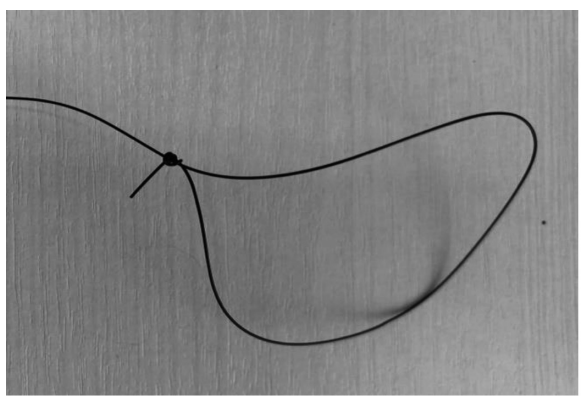


**Figure 5** A sliding knot

## Discussion

Within the realm of sliding knot tying techniques, I favor the application of a straightforward slip knot, demonstrated in Figure 5. This method exhibits exceptional efficacy in securely ligating the cystic duct and its associated vessels across a spectrum of clinical scenarios. The intrinsic value of employing extracorporeal knot ligation becomes particularly apparent in cases characterized by a substantial cystic duct diameter, where alternative approaches to duct ligation may prove arduous to implement with the desired level of confidence. It is imperative to exercise utmost caution when

ligating ducts that exhibit inherent fragility, susceptible to inadvertent disruption. In such instances, it is prudent to explore alternative options to ensure the durable and secure ligation of such delicate ducts.

Laparoscopic cholecystectomy has become the gold standard for gallbladder surgery due to its superior outcomes in terms of hospitalization duration, cost-effectiveness, and patient satisfaction compared to open surgery.[8] Ligation of the cystic duct and vessels demands utmost precision and safety. The extracorporeal sliding knot technique offers several advantages, including simplicity, ease of execution, and comparable stability and safety to other ligation methods involving clips.[9] This technique involves extracorporeally tying a knot and then pushing it down using a specialized knot pusher device, avoiding the complexity associated with intracorporeal knot tying methods.[10-14] The average surgical time of 20 minutes is in line with established standards for LC, indicating efficient procedures at our Medical Center. Additionally, the average hospital stay of 1.5 days reflects effective postoperative care and patient recovery.[15-18] Absence of complications in all cases highlights the proficiency of the surgical team and adherence to established protocols. The shortened hospital stay contributes toimproved patient recovery and cost-effectiveness.

## Limitation

This study's limitations include its retrospective nature, which may lead to potential data inaccuracies and missing information. The single-center design may limit the generalizability of the findings.

## Conclusion

Laparoscopic cholecystectomy with extracorporeal sliding knot using knot pusher technique offers an efficient and safe alternative for cystic duct and vessels ligation during gallbladder surgery. Our study at Mae Fah Luang University Medical Center Hospital demonstrated promising outcomes with reduced surgical time and hospital stay, contributing to enhanced patient satisfaction and cost-effectiveness. This technique holds significant potential as a standard method in laparoscopic cholecystectomy, benefiting patients and medical professionals alike. Further research and long-term follow-ups are warranted to validate and consolidate these findings.

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สำนักวิชาแพทยศาสตร์ มหาวิทยาลัยแม่ฟ้าหลวง
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# Factors Affecting Continuous Follow-up Treatments among Patients Infected with Syphilis at Phramongkutklao Hospital

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**Abstract:**

**Background:** In Thailand, there is an increasing rate of syphilis infection and a recent study found that a significant factor of treatment failure and re-infection was due to a loss of follow-up. Therefore, continuous follow-up is crucial for a successful treatment and to control the disease.

**Objective:** To study factors affecting continuous follow-up treatments among patients infected with syphilis at Phramongkutklao Hospital.

**Materials and Method:** This is a retrospective cohort study of 111 patients diagnosed with syphilis at Phramongkutklao Hospital from 1 January 2012 – 30 April 2022. The results of demographic data, clinical presentations, serology (VDRL, TPHA), sexual behaviour, treatments and follow-up plans are included.

**Results:** From the study, factors significantly affecting continuous follow-up treatments included occupations, domiciles, and presenting conditions. Regarding the domicile factor, patients in the Central part were ten times more likely to continue the follow-up treatments than those in the Southern region (P = 0.045). In comparison to patients who got health check-up or donated blood, patients who firstly diagnosed during antenatal care and those with the presence of neurological symptoms were seven times (P = 0.004) and ten times (P = 0.048) more likely to have continuous follow-up, respectively. In addition, the frequency of patients with other occupations was three times more than soldiers and polices (P = 0.018). Interestingly, among patients who continued their follow-up treatments, most medical professionals failed to complete syphilis treatment follow-up guideline.

**Conclusion:** From this study, potential factors affecting continuous follow-up treatments among patients infected with syphilis included occupation, presenting clinical symptoms, and domiciles. Therefore, these factors should be taken into consideration for the treatment and follow-up plans for patients infected with syphilis.

**Keywords:** Syphilis, Continuous follow-up

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## Introduction

Syphilis is one of the sexual transmission diseases caused by *Treponema pallidum*. There are four stages of syphilis infection including primary, secondary, latent (early and late), and tertiary. Due to different symptoms in each stage, specific treatments, follow-up time, and serological workup are also different. Therefore, continuous and complete serological follow-up is mandatory for accessing treatment outcomes and preventing the spread of infection.[1,2] In order to ensure cure and detect treatment failure or reinfection, treated syphilis patients must be significantly followed up after treatment. This is done by evaluating the clinical and serological response to treatment.

In Thailand, there is an increasing rate of syphilis infection.[3,4] The incidence rate of syphilis in Thailand increases from 2.16 cases per 100,000 person-years in 2010 to 11.51 cases per 100,000 person-years in 2020.[3] A recent study found that significant factor of treatment failure and re-infection was due to a loss to follow-up.[5,6] Therefore, continuous follow-up is crucial for the successful treatment and control of syphilis.

## Materials and Method

### Study design

We conducted a retrospective cohort study from January 2012 to April 2022 including 111 patients who were diagnosed with all stages of syphilis from both inpatient department and outpatient department at Phramongkutklao hospital.

### Inclusion and exclusion criteria

The inclusion criteria were the patients with over the age of 12 years old and the patients who were diagnosed with any stage of syphilis. We excluded the patients who were misdiagnosed. This study was approved by the Research Ethic Committee of Phramongkutklao College of Medicine.

### Definition and data collection

**Continuous follow-up** was defined as the patients who came for every follow-up visit for clinical or serological evaluation according to doctor's appointment.

**Complete follow-up** was defined as the patient who came to follow-up visits following syphilis treatment guideline (table1).

**Table 1** Center for Disease Control and Prevention Recommendations for Follow-up of Adult with Primary, Secondary, Early Latent, or Late Latent Syphilis[7-10]

| Stage of disease | HIV status | Schedule for follow-up after treatment |
|---|---|---|
| Primary or secondary | HIV-uninfected | 6 and 12 months |
| | HIV-infected | 3, 6, 9, 12, and 24 months |
| Early latent | HIV-uninfected | 6, 12, and 24 months |
| | HIV-infected | 6, 12, 18, and 24 months |
| Late latent or latent of unknown duration | HIV-uninfected | 6, 12, and 24 months |
| | HIV-infected | 6, 12, 18, and 24 months |

**Primary and secondary outcome**

The primary outcome was the factor affecting continuous follow-up treatment among patients infected with syphilis and secondary outcome was the rate of continuous follow-up.

**Statistical analysis**

The demographic data were presented as number, mean and percentage. We compared the factors affecting continuous follow-up in patient infected with syphilis using Fisher's exact test, Chi-square test and logistic regression. *P*-value ≤ 0.05 was considered statistically significant.

**Results**

Overall, 111 patients diagnosed with syphilis at any stage were enrolled in the study. The number of female patients were slightly more than male. Most patients had never been infected or received any treatments. No any previously treated patient had followed up according to the syphilis guideline. The demographic data is shown in Table 2.

**Table 2** Demographic data

| Characteristics | Number of patients |
|---|---|
| Number of patients | 111 |
| Sex% (Male: Female) | 45 : 55 |
| Re-infection % (Yes: No) | 5.4 : 94.6 |
| Complete treatment % (Yes: No) | 95.5 : 4.5 |
| Continuous follow-up (Yes: No) | 83 : 28 |
| Complete follow-up | 0 |

The most common age range of the patients was 20-29 years old, and the most common stages of the syphilis infection were late latent and secondary. Human immunodeficiency virus (HIV) was the most common co-infection among patients infected with syphilis. Homosexuality was a common sexual behavior in this study.

Most occupations of the patients were police and soldier. As in table 3, our study revealed that occupation significantly affected continuous follow-up in patients infected with syphilis (P=0.018). The number of patients with other occupations were three times more than soldiers or polices (P = 0.018). The common domicile of the patients was in the central region, and domicile was also a significant factor affecting continuous follow-up in patients infected with syphilis (P=0.033). Regarding the domicile factor, patients in the Central region were ten times more likely to continue the follow-up treatment than those in Southern region (P = 0.045).

The most common abnormal serological report was from antenatal care work up, skin manifestations, health check-up, and blood donation. These factors also affected continuous follow-up of the treatments among patients infected with syphilis (P = 0.002). Compared to those with health check-up or blood donation, patients diagnosed during antenatal care were seven times more likely to have continuous follow-up (P = 0.004). With neurological symptoms, patients infected with syphilis were ten times more likely to visit for continuous follow-up (P = 0.048).

**Table 3** Factors affect continuous follow-up in patients infected with syphilis

| Characteristics | Non-continuous F/U | Continuous F/U | P-value |
|---|---|---|---|
| Age | | | |
| Less than 20 years | 6 | 11 | 0.39 |
| 20 – 29 years | 15 | 39 | |
| 30 – 39 years | 5 | 17 | |
| More than 40 years | 2 | 16 | |
| Gender | | | |
| Male | 17 | 22 | 0.088 |
| Female | 11 | 50 | |
| Occupations | | | |
| Soldiers/Polices | 11 | 14 | 0.018 |
| Governments | 1 | 2 | |
| Business owner | 2 | 6 | |
| Employee | 2 | 17 | |
| Student | 5 | 5 | |
| Unknown | 7 | 39 | |
| Domiciles | | | |
| Central | 17 | 61 | 0.033 |
| Northeast | 5 | 7 | |
| Southern | 3 | 1 | |
| Eastern | 2 | 2 | |
| Presenting conditions | | | |
| Skin | 9 | 9 | 0.002 |
| Antenatal care | 6 | 41 | |
| Other STDs* | 4 | 8 | |
| Neurological symptom | 1 | 10 | |
| Check-up / blood donation | 8 | 8 | |
| Complete medication | | | |
| Incomplete | 1 | 2 | 0.562 |
| Complete | 25 | 81 | |
| Co-infection with HIV | | | |
| Yes | 5 | 20 | 0.673 |
| No | 23 | 63 | |

*STDs, Sexually Transmitted Diseases

Logistic regression predicting continuous follow-up: Comparing between non soldiers or polices and soldiers or polices: between other regions and southern region: between other presenting conditions and health check-up or blood donation was shown in table 4, 5 and 6 respectively.

**Table 4** Logistic regression predicting continuous follow-up: Comparing between non soldiers or polices and soldiers or polices

| OR (95%CI) | P (Wald 's test) | P (LR-test) |
|---|---|---|
| 3.19 (1.23,8.23) | 0.017 | 0.018 |

**Table 5** Logistic regression predicting continuous follow-up: Comparing between other regions and southern region

| Region | OR (95%CI) | P (Wald 's test) |
|---|---|---|
| Central | 10.76 (1.05, 110.21) | 0.045 |
| Northeast | 4.2 (0.33, 53.12) | 0.268 |
| Eastern | 3 (0.15, 59.89) | 0.472 |

**Table 6** Logistic regression predicting continuous follow-up: Comparing between other presenting conditions and health check-up or blood donation

| Presenting condition | OR (95%CI) | P (Wald 's test) |
|---|---|---|
| Antenatal care | 6.83 (1.86, 25.12) | 0.004 |
| STD* | 2 (0.42, 9.42) | 0.381 |
| Neurological symptoms | 10 (1.03, 97.5) | 0.048 |
| Skin manifestation | 1 (0.2601, 3.8453) | 1 |

*STDs, Sexually Transmitted Diseases

## Discussion

Previous studies had revealed that the follow-up loss in patients infected with syphilis increased the incidence of treatment failure and re-infection.[5] Therefore, lost follow-up was an essential factor in the treatment outcomes and control of syphilis infection. However, there have been no previous studies on factors affecting continuous follow-up in patients infected with syphilis. In this study of 111 patients infected with syphilis, significant factors affecting continuous follow-up were occupations, domiciles, and presenting conditions. Possible explanations of soldiers and polices who are more likely to lose follow-up are their occupations, which might be related to their missions or duties. In addition, patients from the Central region who visited for continuous follow-up more

than those from Southern region are likely due to the location of Phramongkutklao Hospital, which is more convenient to them.

Presenting conditions were also a significant factor affecting continuous follow-up. Patients who were diagnosed with syphilis during ANC or had neurological symptoms were more likely to visit for continuous follow-up treatments than those diagnosed during health check-ups or blood donation. Those patients diagnosed during ANC might have more concern about the health effects of syphilis infection on their babies. Patients with neurological symptoms also had concurrent physical abnormalities which required continuous intensive medical care. Therefore, the patients who were aware of their health conditions, consequently, were likely to follow the medical recommendation including the clinical monitoring.

Interestingly, none of the patients visited for complete follow-up treatment according to the syphilis guideline, partly due to the improvement of their symptoms and no appointment from the doctor after non-reactive of nontreponemal test were shown. Therefore, health education and awareness were crucial for patients infected with syphilis to visit for continuous follow-up and completed follow-up. The encouragement for complete follow-up according to the syphilis guideline to the doctor was important, although the clinical and serological examinations were normal.

Finally, we suggest that establishment of a sexually transmitted disease clinic and generation of a syphilis information sheet may encourage patients infected with syphilis to visit for continuous follow-up and complete follow-up for controlling of syphilis.[11-15]

Limitations of our study included the small sample size and retrospective study design with some incomplete medical records.

## Conclusion

Our study showed significant factors affecting continuous follow-up in patients infected with syphilis comprised domicile, occupation, and presenting conditions including during antenatal care, suffering from neurological symptoms. Therefore, these factors should be taken into consideration for the treatment and follow-up plan for patients infected with syphilis.

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Case Report

GMSMJ

Greater Mekong Subregion Medical Journal

# Percutaneous Coronary Intervention in Patient with Protein C Deficiency

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**Abstract:**

The incidence of acute STEMI in patients with protein C deficiency is rare. Treatment of acute STEMI in patients with coagulation disorders is like that of the general population. Medication after the occluded artery has been performed by balloon and stent placement, especially for patients who take direct oral anticoagulants (DOACs) and still have thromboembolism. It is something that needs to be planned for treatment and further study.

**Keywords:** Acute STEMI, Protein C deficiency, Percutaneous Coronary Intervention

## Introduction

The incidence of acute coronary syndrome (ACS) in developed countries tends to decrease due to the control of risk factors.[1,2] For Thailand, there is a tendency for deaths from ACS to increase steadily every year. In 2011 there was a death rate of 22.5 per 100,000 population, rising to 31.8 in 2017. However, the mortality rate in hospitals, especially ST-elevation myocardial infarction (STEMI) patients, decreased steadily from 17% in 2002 to about 10% in 2018.[3]

Acute ST-segment elevation myocardial infarction (STEMI) in the context of protein C deficiency is a rare. Protein C deficiency is a medical condition that affects blood coagulation and is considered an inherited thrombophilia, which means there is an increased tendency to develop abnormal blood clots. Protein C is a natural anticoagulant that regulates blood clotting and prevents excessive clot formation. When a blood vessel is injured, complex reactions occur to form a blood clot, which helps stop bleeding. However, this clotting process must be carefully balanced to prevent excessive clot formation, which can lead to harmful blockages in blood vessels (thrombosis).[4] When it occurs in the setting of acute STEMI, it can further complicate in management of the condition. In individuals with protein C deficiency, there is a reduced amount or impaired function of protein C, making it harder to regulate the clotting process. This deficiency can be either congenital (inherited from one or both parents)[5] or acquired (developed later in life due to other medical conditions or treatments).[6] Symptoms and complications of protein C deficiency can vary from mild to severe. They may include deep vein thrombosis (DVT), pulmonary embolism

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(PE), skin necrosis, and increased risk of miscarriage in pregnant women.[7-10]

Treatment for protein C deficiency aims to prevent clot formation. It may involve anticoagulant medications such as warfarin or direct oral anticoagulants (DOACs).[11,12] Supportive measures such as compression stockings may be recommended to improve blood flow in the legs and reduce the risk of DVT.[13]

## Case report

A 44-year-old man presented with acute cardiac chest pain for about three hours. He had underlying ischemic stroke, protein C deficiency, hypertension and dyslipidemia. Current medications included Apixaban (5 mg) 1 tab orally BID pc, Manidipine (20 mg) 1 tab orally OD pc, Losartan (100 mg) 1 tab orally OD pc, and Atorvastatin (40 mg) 1 tab orally OD HS. Physical examination revealed an unremarkable study. Electrocardiography (ECG) showed ST segment elevation at II, III, and aVF as in Figure 1. Echocardiography showed inferior wall hypokinesia, no valvular heart disease with LVEF 61%. Coronary angiography showed an occluded lesion at the right coronary artery (RCA) as in Figure 2. The left coronary artery was not shown obvious stenosis. The RCA was engaged with a 6-French extra-backup catheter (RBU3.5), and then a Runthrough hypercoat wire (Terumo) was passed to the distal part of the RCA. PCI was done using a Sapphire II pro balloon 2.0 × 20 mm and Terumo Ryurei SC balloon 3.0 × 20 mm pre-dilatation at mid to distal RCA lesion. IVUS showed many intraluminal thrombi with minimal plaque at the endothelium. Blood clot was removed by a Thrombuster Pro catheter. The mid to distal RCA lesion was stented with 4.0×9 mm, 3.5 × 36 mm, and 3.5 × 19 mm Biometrix alpha stents. Post stent angiogram shows in Figure 3.

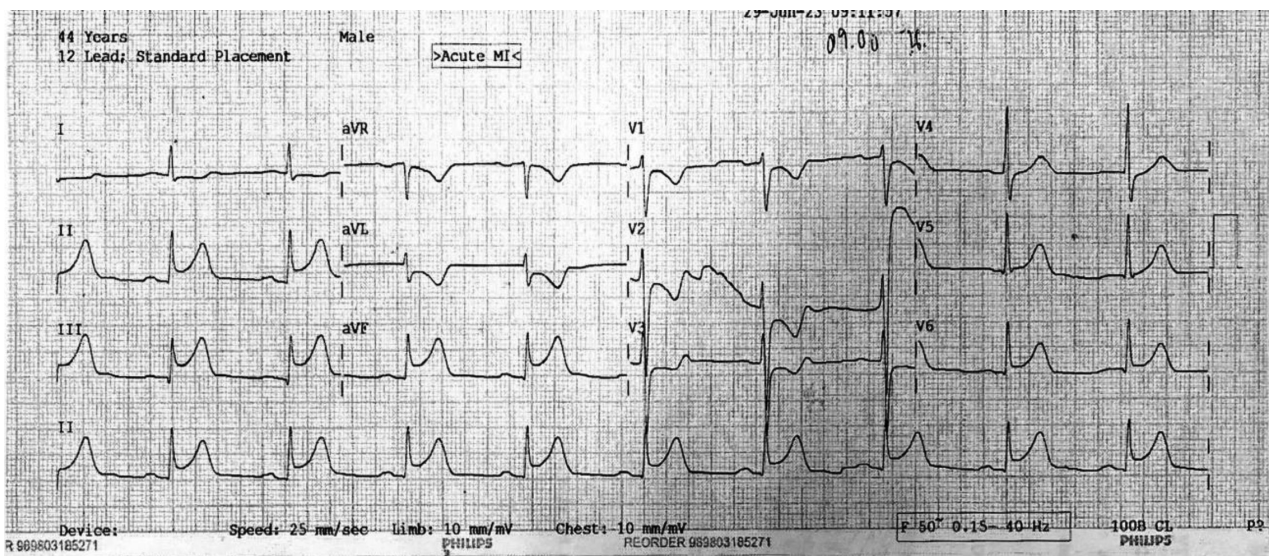


**Figure 1** ECG shows ST segment elevation at II, III, and aVF

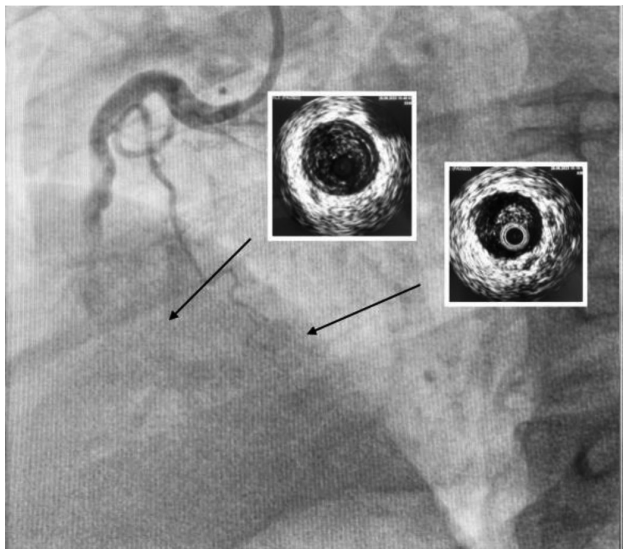

**Figure 2** Coronary angiography shows occluded lesion at the right coronary artery (RCA)

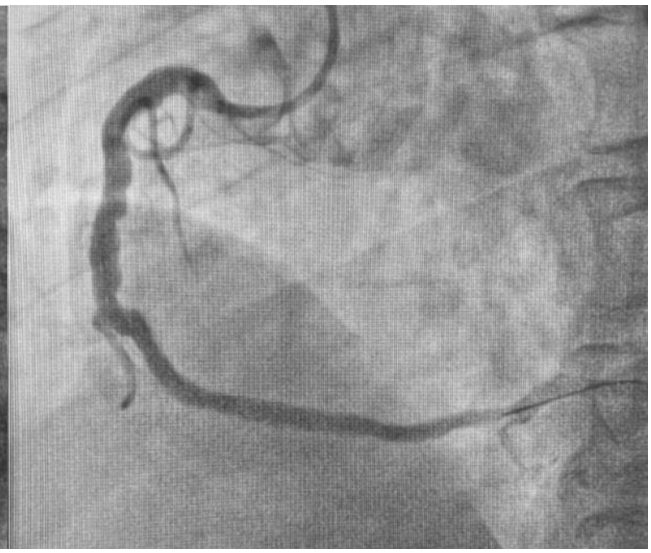

**Figure 3** Post stent angiogram

## Discussion

Acute ST-segment elevation myocardial infarction (STEMI) is a severe form of heart attack characterized by complete or near-complete occlusion of a coronary artery, resulting in the death of heart muscle (myocardium) due to a lack of blood supply.[14] The pathophysiology of STEMI involves several key processes.[15,16] Early intervention can significantly improve outcomes and reduce the risk of complications.[17]

Acute ST-segment elevation myocardial infarction (STEMI) in the context of protein C deficiency is a rare and complex situation. Protein C deficiency is an inherited or acquired disorder that affects the body's ability to regulate blood clotting.[18] When it occurs in the setting of acute STEMI, it can further complicate the pathophysiology and management of the condition. Here's how protein C deficiency may contribute to the development and progression of acute STEMI:

1. Hypercoagulability: Protein C is a natural anticoagulant protein that plays a crucial role in inhibiting blood clot formation. Its deficiency can lead to a prothrombotic state, making individuals more prone to developing blood clots, including those that can cause a STEMI.

2. Increased thrombus formation: In protein C deficiency, there is a higher likelihood of forming blood clots, especially in situations where there is atherosclerosis and plaque rupture, as seen in STEMI. The reduced ability to control clot formation can result in more extensive and occlusive thrombi within the coronary arteries.

3. Impaired fibrinolysis: Protein C deficiency can also affect the fibrinolytic system, which is responsible for breaking down blood clots. This impairment can make it challenging to dissolve or break apart the thrombus once it forms, further exacerbating the blockage in the coronary artery.

4. More severe clinical presentation: The combination of protein C deficiency and acute STEMI may lead to a more severe clinical presentation, with larger infarct size, increased risk of complications, and potentially worse outcomes.

5. Management challenges: Protein C deficiency poses unique challenges in the management of acute STEMI. Traditional anticoagulant therapies like heparin or

antiplatelet agents may need to be carefully adjusted or supplemented to address the underlying coagulation disorder.

Management of acute STEMI in individuals with protein C deficiency typically involves a multidisciplinary approach, including cardiologists and hematologists. The treatment may involve anticoagulant medications that are specific to protein C deficiency, in addition to standard therapies for STEMI, such as reperfusion strategies like PCI or thrombolytic therapy.[19]

DOACs (Direct oral anticoagulants) are a class of medications used to prevent and treat blood clots. They work by inhibiting certain clotting factors in the blood, thereby reducing the risk of clot formation. The DOACs include dabigatran, rivaroxaban, apixaban, and edoxaban. The connection between DOACs and protein C deficiency lies in the mechanism of action of these medications. DOACs inhibit specific clotting factors like thrombin (dabigatran) or factor Xa (rivaroxaban, apixaban, edoxaban) to prevent clot formation. However, this inhibition may exacerbate the underlying tendency to bleed in individuals with protein C deficiency, as they already have a reduced ability to regulate clotting.[12] For individuals with protein C deficiency, anticoagulant therapy requires careful consideration. Traditional anticoagulants like warfarin, which target multiple clotting factors (including vitamin K-dependent factors like protein C), have been used cautiously in these patients. The management of anticoagulation in protein C deficiency is often complex and individualized, considering factors like the severity of the deficiency, the clinical context, and the risk of bleeding versus clotting.[20]

It is essential for individuals with protein C deficiency to work closely with their healthcare provider, preferably a specialist in hematology or thrombosis, to determine the most appropriate anticoagulation strategy for their specific case. Close monitoring and regular follow-up are necessary to optimize treatment outcomes and minimize potential risks.

## Conclusion

Percutaneous coronary intervention (PCI) for obstructive lesion in protein C deficiency is uncommon. Long-term anticoagulant is still necessary in patients with protein C deficiency.

## Potential conflicts of interest

The author has no relevant conflict of interest to disclose.

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**Short Communication** **GMSMJ** **Greater Mekong Subregion Medical Journal**

# A Case of *Streptobacillus moniliformis* Bacteremia with IIiopsoas Abscess

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## Abstract:

*Streptobacillus moniliformis* is a Gram-negative bacillus usually colonized by rodents and causes rat bite fever as a zoonotic infection; however, it is unusual to develop *S. moniliformis* infection without a history of contact with rodents. Here we report an 87-year-old patient with no history of direct contact with rodents who developed *S. moniliformis* bacteremia with iliopsoas abscess. She had low back pain, and her CT scan showed a left iliopsoas abscess and an aortic aneurysm dissection, Stanford type B. Blood culture was positive for unidentifiable Gram-positive bacillus and finally confirmed to be *S. moniliformis* by ribosomal RNA homology analysis. She was treated with intravenous tazobactam/piperacillin, followed by oral amoxicillin. We should mention that *S. moniliformis* infection can be developed without rodent contact.

**Keywords:** *Streptobacillus moniliformis*, iliopsoas abscess

## Introduction

*Streptobacillus moniliformis* is a Gram-negative bacillus with a highly pleomorphic stainability on Gram staining. *S. moniliformis* was mainly colonized with rodents such as rats and caused rat bite fever (RBF) by infection through a bite by rodents and oral infection through contaminated foods.[1] Here, we report a rare case of

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*S. moniliformis* bacteremia with iliopsoas abscess without apparent contact with rodents.

**Case**

An 87-year-old female was consulted from previous hospital with the complaint of back pain. Laboratory testing revealed highly C-reactive protein level as 28.98 mg/dL, and magnetic resonance imaging (MRI) indicated lumbar spondylosis, resulting in our hospital admission. Three days after admission, she developed fever, and imaging computed tomography (CT) revealed a spot in her left iliopsoas (Figure 1). Iliopsoas abscess was suspected, and administration of 2 g/day of sulbactam/cefoperazone was started after taking blood culture samples.

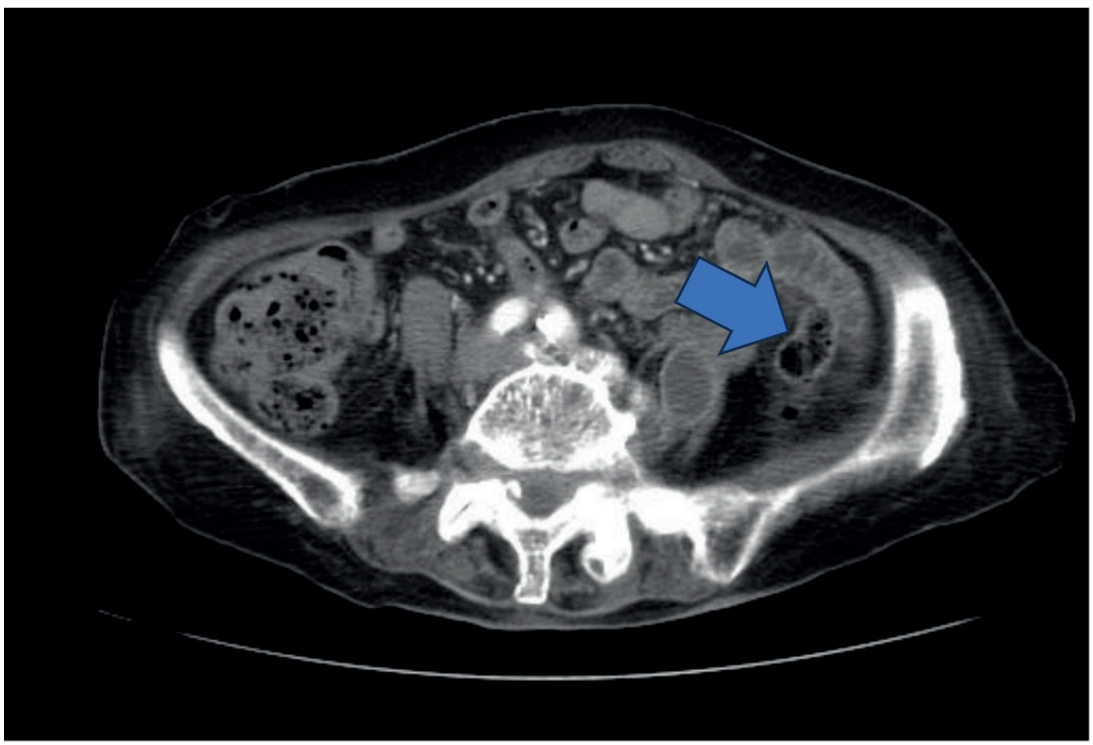

**Figure 1** Abdominal imaging Computed tomography findings. The blue arrow indicated iliopsoas abscess.

Her blood culture samples taken in her previous hospital were sent to an external commercial laboratory and cultured by BAC TEC FX (Becton Dickinson), and Gram-positive bacillus was identified. The bacteria was subcultured with 5% $CO_2$ conditions at 35°C using 5% blood agar media. Identification of the bacteria with matrix-assisted laser desorption ionization time-of-flight mass spectrometry (MALDI-TOF MS) resulted in failure, so the commercial laboratory reported the result of bacterial testing to her previous hospital as "unidentifiable Gram-positive bacillus was positive for the blood culture" with antibiotics sensitivity testing result (Table 1) of the bacteria at nine days after admission.

**Table 1** Susceptibility testing result of *Streptobacillus moniliformis*

| Antimicrobial agents | Minimum inhibitory concentration (μg/ml) | Interpretation of breakpoint* |
|---|---|---|
| Benzylpenicillin | ≤0.5 | S |
| Ampicillin | ≤0.5 | S |
| Sulbactam/ Ampicillin | ≤8 | S |
| Cefmetazole | ≤16 | S |
| Ceftriaxone | ≤16 | S |
| Flomoxef | ≤16 | S |
| Cefepime | ≤16 | S |
| Imipenem/Cilastatin | ≤4 | S |
| Meropenem | ≤4 | S |
| Erythromycin | ≤2 | S |
| Clindamycin | ≤1 | S |
| Minocycline | ≤4 | S |
| Vancomycin | ≤1 | S |
| Levofloxacin | ≤2 | S |

*S, susceptible. The breakpoints were interpreted according to the Clinical and Laboratory Standards Institute document M100, Performance Standards for Antimicrobial Susceptibility Testing, 23rd ed.

Then, antibiotic was changed to tazobactam/piperacillin (TAZ/PIPC) (4.5 g every six hours) based on the results of the antibiotics sensitivity test 9 days after her admission. However, she was transferred to our hospital ten days after admission because an imaging CT performed eight days after admission revealed her dissection aortic aneurysm (Stanford type B). Imaging CT performed in our hospital also indicated her remaining iliopsoas abscess (Figure 1) and her dissection aortic aneurysm. Administration of TAZ/PIPC was continued, and antihypertensive therapy was started against her dissection aortic aneurysm. An imaging CT performed 25 days after admission revealed shrinking iliopsoas abscess, and her condition tended to improve without exacerbating of aortic dissection aneurysm. So, antibiotics was changed to amoxicillin (AMPC) (250 mg every eight hours) 31 days after admission, and finally, she was discharged from our hospital 84 days after admission.

We ordered the bacterial strain from the external commercial laboratory to identify the bacteria isolated from her blood culture sample. The bacteria were Gram-negative bacillus with pleomorphic shape (Figure 2) and identified as *S. moniliformis* by MALDI biotyper (BRUKER) with high reliability (score value = 2.438). 16S Ribosomal RNA (rRNA) homology analysis of the bacteria was performed in Yamagata Prefectural Institute of Public Health, and nucleotide sequence of 1,400 bp amplicon derived from

the bacteria (accession no. LC441154.1) showed 100% homology with *S. moniliformis* strain ATCC 14647 (accession no. 599252.1).

## Discussion

*S. moniliformis* is the causative bacterium of RBF, and between 50 and 100% of rats are colonized in the nasopharynx.[1] *S. moniliformis* infections mainly occur through rat bite but are also associated with the ingestion of contaminated food or water.[1] RBF is a systemic illness generally characterized by fever, rash, and polyarthralgias.[1] A variety of severe complications of RBF such as bacteremia, endocarditis, focal abscesses, septic arthritis, and multiorgan failure have been reported.[2–6] If not treated appropriately, the mortality rate of RBF is approximately 13 percent.[1] The present case was characterized by *S. moniliformis* bacteremia with iliopsoas abscess. Iliopsoas abscess is extremely rare as a complication of *S. moniliformis* infection. To the best of our knowledge, there is no other report of *S. moniliformis* infection with abscess in muscle tissue except for a previous case report[7] and the present case. Three to six weeks of antibiotic treatment following adequate drainage against iliopsoas abscess is empirically recommended in general, whereas there was no clear guideline for the treatment of the disease. Penicillin is first choice antibiotic of RBF.[1] and prompt treatment can prevent severe complications. In the present case as well, TAZ/PIPC and AMPC were successful in patients with iliopsoas abscesses.

In the present case, the patient had no history of rat bites or apparent contact with rats. According to our retrospective interview with the patient, she had frequently seen rodents in her old house. This fact suggests a possibility that she infected *S. moniliformis* through food or water contaminated by rat excrement. This finding is supported by some previous reports that caused *S. moniliformis* bacteremia without rat bite.[8,9] In addition, consistent with our patients, approximately 30% of the patients could not recollect any bite or other exposure.[10] In the present case, due to the lack of rat bite history of the patient, it was difficult to take into account the possibility of RBF. When outpatients lack specific clinical findings of RBF, detailed interviews, including about their living environment, would lead to considering *S. moniliformis* infection.

When there was no history of rat bites or contact with a rat for the patient, the diagnosis of *S. moniliformis* infection will be based on microbiological testing. However, microbiological diagnosis of *S. moniliformis* is also difficult because *S. moniliformis* is known as a fastidious bacterium. In the present case, the external commercial laboratory reported the result of blood culture as "unidentifiable Gram-positive bacillus was detected," whereas *S. moniliformis* is Gram-negative bacteria. Indeed, the Gram-staining we performed using subcultured colonies showed the bacteria as Gram-negative (Figure 2). This mismatch of findings accounts for the characteristic of *S. moniliformis* as a highly pleomorphic stainability on Gram staining.[11] Hence, the stainability of *S. moniliformis* on Gram staining should be paid attention to, especially when the bacterium was detected from the blood culture.

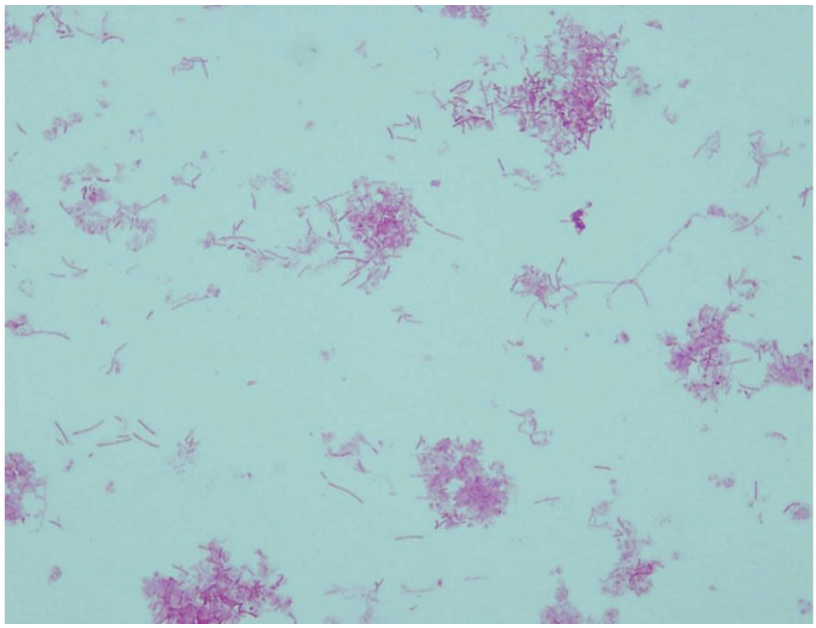

**Figure 2** Pleomorphic shaped Gram-negative rods were shown on Gram staining (×1,000)

Microbiological identification of *S. moniliformis* is also difficult. In the present case, MALDI-TOF MS was performed in the commercial laboratory, where her previous doctor used could not identify this bacterium. MALDI-TOF MS is a fast and reliable tool for species identification of *S. moniliformis*[12] whereas whether the device can identify *S. moniliformis* or not depends on the type of device and database the device possessed. Because of the difficulty in microbiological identification of RBF, 16S rRNA gene sequencing has developed to identify *S. moniliformis*.[12] If *S. moniliformis* cannot be identified by MALDI-TOF MS, while we were able to identify this organism, fortunately, using 16S rRNA gene sequencing is desired for the identification of this bacterium. On the other hand, 16S rRNA gene sequencing can be insufficient for definite species resolution because of the highly homologous against *S. moniliformis*, Streptobacillus felis, Streptobacillus notomytis, and Streptobacillus ratti[12], contrary to MALDI-TOF MS. Hence, using MALDI-TOF MS on routine work and if necessary, using 16S ribosomal RNA gene sequencing in combination makes the diagnose of *S. moniliformis* infection definitive. In order to identify *S. moniliformis* using MALDI-TOF MS more definitely, modification difference between devices and improvement database the device possessed are needed.

The patient had an aortic dissection aneurysm with *S. moniliformis* infection, but the relationship between the aneurysm and *S. moniliformis* infection was unclear. Aortic dissection can generally be triggered by an infectious aneurysm.[13] The fact that infectious aneurysms can occur by the seeding of bacteria[13] leads to a possibility that bacteremia with *S. moniliformis* is involved in the development of aortic dissection in this case. In contrast, no previous report of *S. moniliformis* infection with infectious aneurysms was reported. However, we cannot further discuss these relationships here because the patients have not been treated surgically in this case.

Management of iliopsoas abscess consists of drainage and prompt initiation of appropriate antibiotic treatment.[14] However, drainage from the iliopsoas abscess site was impossible in this case because of her aging and concerns about worsening her aortic dissection aneurysm. Hence,

this case was clinically diagnosed as *S. moniliformis* bacteremia with iliopsoas abscess associated based on isolated *S. moniliformis* from blood culture only. If *S. moniliformis* had been directly detected from the iliopsoas abscess, the diagnosis of iliopsoas abscess accompanied by *S. moniliformis* bacteremia would have been more reliable.

## Conclusion

We report the rare case of *S. moniliformis* bacteremia with iliopsoas abscess without apparent contact with the rat. Iliopsoas abscess is a rare complication of *S. moniliformis* infection. A detailed interview about the possibility of contact with rats and the presence of rats in the patient's living environment is important. Although clinically diagnosing *S. moniliformis* infection without a rat bite is difficult, laboratory testing combining MALDI-TOF MS with 16S rRNA gene sequencing helps a more definitive diagnosis of *S. moniliformis* infection.

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Review Article

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# Post-Mortem Investigation at the Scene of Death in Thailand

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**Abstract:**

Investigating a scene of death is a legal procedure that require the participation of medical professionals and cannot be avoided. This article aims to provide essential information about the basic procedures for investigating a crime scene and conducting a post-mortem examination in accordance with Thai laws, to ensure that readers can perform their jobs correctly and with confidence. The topics covered include the reasons for conducting a post-mortem examination according to Section 148 of the Criminal Procedure Code, the role of physicians and the post-mortem examination team, the preparation process before post-mortem examinations, data inquiry when a doctor arrives at the location where a corpse is found, techniques for photographing and collecting evidence, the forensic examination of a corpse, how to evaluate the time of death using rigor mortis, livor mortis, and the stages of decomposition, and recommendations for providing detailed feedback on post-mortem examination reports. In summary, examining the scene of death is a necessary procedure that all doctors must be able to carry out within the framework of the law. It is an important mechanism for promoting justice in society, relying on medical and scientific knowledge for the benefit of the general public.

**Keywords:** Corpse; Crime Scene; Criminal Procedure Code; Post-Mortem Examination

## Introduction

The process of investigating a crime scene and conducting a post-mortem examination is a legal procedure, in which medical professionals are necessary to participate and cannot be avoided. In many homicide cases, it is necessary to rely on evidence obtained from the investigation of the crime scene and the autopsy to convict the perpetrator. Sometimes, this can lead to the exoneration of the accused. This article will present essential information about the basic procedures for investigating a crime scene under the Thai laws, to ensure that readers have confidence and can perform their jobs correctly.

## Reasons for Conducting Post-Mortem Examinations

According to Section 148 of the Criminal Procedure Code, "When it is clear or suspected that a person has died unnaturally, or died while in the custody of

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an officer, a post-mortem examination shall be conducted, unless the death was caused by lawful execution.

Death by unnatural causes means:

1. Suicide.
2. Homicide.
3. Death by animal attack.
4. Death by accident.
5. Death by unknown causes."[1]

In accordance with this provision, in cases of death by unnatural causes, which include the five aforementioned circumstances, it is necessary to conduct a post-mortem examination at the location where the incident occurred. Similarly, in cases where death occurs while in the custody of an officer, such as in prison or while under arrest, it is necessary to conduct a post-mortem examination at the location where the incident occurred.

## Physicians and the Post-Mortem Examination Team

Physicians in government hospitals are considered government officials according to the Criminal Code, Section 1 (16), which defines "government officials" as individuals who are legally established or appointed by law to perform official duties, whether regularly or occasionally, and regardless of whether they receive compensation or not. Therefore, if a doctor fails to perform his or her duties as assigned, he or she may be liable under the Criminal Code, Section 157, which states that "Any government official who performs or fails to perform his or her duties without authorization, causing damage to another person, or who performs or fails to perform his or her duties dishonestly, shall be punished with imprisonment from one year to ten years or a fine from twenty thousand THB to two hundred thousand THB or both."[2]

However, doctors can delegate the task of attending post-mortem examinations to hospital staff or staff of the Provincial Public Health Office who have received legal medical training only in cases of death under the Criminal Code Sections 148 (3), (4), and (5)."[3,4]

## Preparing Before Post-Mortem Examinations

When notified by investigators to attend a post-mortem examination procedure, medical personnel must prepare various equipment before traveling to the scene, including equipment necessary for the current situation, such as:

1) Recording and document signing equipment, such as pens, personal computers, and printers (in case of printing reports) and others.

2) Photography equipment (DSLR camera recommended).

3) Measuring equipment for object length, such as rulers, steel tapes, and laser distance meters.

4) Personal protective equipment, such as rubber gloves, shoe covers, respirators, and face and eye protection equipment.

5) Equipment for collecting samples for examination, such as syringes, blood collection tubes, cotton swabs, plastic bottles, paper bags, scissors, and scalpels.[5]

Always remember that medical personnel must assess the safety of the scene first. If it is determined that it is dangerous for themselves, such as collapsed buildings, fire, deaths in poorly ventilated areas, and deaths on the road without cordoned off areas to prevent danger from vehicles, then should refrain from examining the body until it is confirmed safe to enter the area. If it is not possible to do so, the person responsible for ensuring the safety of the scene should take photographs of the body and then move it to a safe area for further examination.

**Data Inquiry**

When a doctor arrives at the location where a body is found, they should conduct a preliminary inquiry with the person who witnessed the event or the person who found the body first. The objective is to obtain information about the cause of death, similar to taking a patient's medical history. However, unlike a patient, the deceased cannot provide information about the incident. Therefore, the doctor should ask about the following topics:

1) Name and surname of the deceased.

2) Who was the deceased? What was their occupation? Where did they live? Did they have any underlying medical conditions?

3) Who is the person answering the questions? How are they related to the deceased?

4) Describe the events that occurred from before the deceased's death until after their death (if witnessed).

5) The last time the deceased was seen and what they were doing at that time.

6) Was the body moved or handled in any way? If so, how?

7) If foul play is suspected, inquire about the motive and weapon used in the incident.

8) If the information provided does not match the evidence found on the body or at the scene, ask the person providing the information to explain the reason for the discrepancy.

During the process of questioning witnesses, if there are multiple witnesses present, it is recommended to question at least two of them to verify whether their information is consistent or not. At the same time, doctors must observe the characteristics of the information providers to determine whether they are providing false information or not. Testing for deception by comparing human behavior with the use of robots to detect deception has shown that the results trend in the same direction.

1) Eye movements: Individuals who lie have a tendency to have wider pupil dilatation than those who tell the truth.

2) Time to respond: Individuals who lie have a tendency to answer questions more slowly than those who tell the truth.

3) Eloquence: Individuals who tell the truth have a tendency to speak more eloquently than those who lie.[6]

**Photographing the Scene and Collecting Evidence**

When taking photographs, the image should be captured from a wide-angle view, then specific details should be captured to the fullest extent possible, including:

1) The entrance to the crime scene and the surrounding area.

2) The condition of the area where the body was found.

3) Various household items.

4) Medicines used to treat diseases.

5) Evidence found at the scene of death.

6) The condition of the body, and so on.

Once the crime scene has been manipulated, it is not possible to go back and take pictures as before. Therefore, if there is equipment to measure the length of an object, it should be placed next to the object to be photographed horizontally. It should not be photographed from a perspective view, as it will not reveal the true proportion of the length of the object when compared to the measuring instrument.

As for the collection of evidence at the crime scene, the assistance of a physician may be necessary to collect and examine the evidence. Recommendations for practice include leaving samples to dry before packing them in paper envelopes, to make it easier for the humidity to be transmitted, and to leave samples to dry before packing them in bags. As for the principles of forwarding evidence, they use "Chain of Custody," and the evidence should be kept

in a safe place and only be accessible to authorized personnel. The details that should appear on the packaging of evidence are as follows:

1) Clearly specify the type or category of the evidence.

2) Name and signature of the person who collected the evidence.

3) Office number and contact information.

4) Name of the recipient of the evidence.

5) Name and address of the laboratory.

6) Date and time of collection and/or analysis.

7) Method of analysis.

8) Signature of all individuals involved in the process, including the date and time.[7]

If the evidence is not handled completely and correctly at any stage of the transfer process, such as opening the container by an unrelated person who did not sign, it may affect the credibility of the evidence and the consideration of the case in court.

**Forensic Examination of a Corpse**

Once the crime scene has been properly photographed, the next step is to examine the condition of the body, with the following important details:

1) Photograph the outside of the body, then photograph to identify the characteristics of the person such as clothing, jewelry, skin color, hair style, and other evidence at the scene.

2) Photograph wounds or bruises in all parts of the body that can be examined. The photo should be clear enough to identify the location of the wound, such as a laceration on the left arm. At least one photo should be taken, then details of the wound should be photographed up close while measuring the length of the object (if any) placed parallel to the wound.

3) Take photos from head to toe, including the face, eye tissues, arms, hands, legs, and feet, as well as the front and back of the body.

When examining the crime scene, the forensic physician should always keep in mind that what is seen may not be the truth. In this case, there are some important points to consider when examining a corpse, such as:

1) Examination of eye tissues: In cases where death was due to lack of oxygen, petechial hemorrhages may be found under the eye tissues, due to pressure on the neck and jugular veins. However, petechial hemorrhages may also be found under the eye tissues after death, especially in cases where the body was lying face down.

2) Examination of children's bodies: Forensic physicians should ask for clear medical history. If there is no underlying disease that may have caused the death, the examiner should take into account factors such as the age, size, and developmental stage of the child.[8]

3) Examination of the body of a deceased person from gunshot wounds and explosions: Since the examination of the body at the scene of the incident is to assess the preliminary cause of death and may not be able to answer legal doubts in all aspects, the body should be sent for autopsy to examine the injuries in detail.

**Evaluation of the Time of Death**

According to the hot weather in Thailand, the measurement of the change in body temperature after death (algor mortis) is not very useful. The following are commonly used methods for assessing the time of death:

1) Rigor mortis (the stiffening of muscles after death):

a. Usually appears about 3 hours after death or may occur earlier. It is easily observed in small muscles such as fingers, toes, and jaws.

b. It then becomes apparent in large muscles such as elbows, shoulders, knees, and finally in the hip joint, fully stiffening about 6-12 hours after death.

c. If there is movement in the joints of the body before rigor mortis sets in, it may occur in the muscles that have not fully developed rigor mortis. However, if there is movement in the joints after rigor mortis has fully set in, rigor mortis will not occur again.

d. Caution should be taken during the examination to differentiate between muscles that are only partially stiff due to the development of rigor mortis and those that are not fully stiff due to the decomposition process. Other characteristics of the body should be observed as well.[5]

2) Livor mortis (the settling of blood in the lower parts of the body after death):

a. Livor mortis occurs due to the settling of blood to the lowest point of the body after death. These methods can provide important information for determining the time of death, but other factors such as the environment, cause of death, and individual differences should also be considered. It usually appears about 0.5-2 hours after death. In the early stages, if pressure is applied to the affected area, the color of livor mortis will fade. The color will gradually darken over time.

b. The color of livor mortis becomes fully pronounced about 8-12 hours after death.

c. In most cases, it is usually not possible to fade Livor mortis within 12-24 hours after death.[5]

3) Decomposition: Can be divided into 5 stages:

a. Fresh stage: This stage occurs at the beginning of decomposition and often exhibits greenish discoloration on the skin of the lower right abdomen due to the occurrence of livor mortis and rigor mortis, which typically appears about 18 hours after death. However, from the experience of the author, this may not always occur in the lower right abdomen and may become visible after a longer period of time. For example, in some cases, it may begin to appear 24 hours after death.

b. Bloated stage: This stage is characterized by the appearance of blisters on the skin, skin slippage, marbling, and bloating, which typically begin to appears approximately 24-48 hours after death.

c. Active decay: Hair sloughing and slippage of the scalp skin occurs. The underlying tissue becomes discolored with black pigmentation.

d. Advanced decay: This stage is characterized by the loss of muscle tissue, leading to the appearance of bones.

e. Skeletal stage: At this stage, the bones are clearly visible and show signs of fractures. Soft tissues, ligaments, and cartilage are minimally present.[9]

From the author's experience, the bloated stage usually occurs between 36-72 hours after death, while active decay is typically observed 5-7 days after death. However, it is difficult to assess the time frame of advanced decay and skeletal stage due to the variability of environmental factors and the length of time since death, and therefore requires additional information and evaluation.

## Recommendations for Providing Detailed Feedback on Post-Mortem Examination Reports

The recommendations for writing any details on the post-mortem examination reports are shown below.

1) Describe the general condition of the body, such as sex, skin color, hair color, body shape, defects, tattoos, clothing, posture at the time of death, and general location details.

2) Describe findings such as external injuries, rigor mortis, dependent lividity, and putrefaction (if present).

3) Estimate the time of death by providing a time range, such as 2-4 hours.

4) Use the word "suspected" when assessing the cause of death since it is only a preliminary assessment.

5) Normally, Thai doctors do not include the manner of death about the deceased, but if the doctor is very confident, they can indicate it.

6) Provide opinions on how to handle the body, such as whether to hand it over to family members for religious ceremonies or perform an autopsy to investigate the cause of death.

## Conclusion

In summary, examining the scene of death is necessary procedures that all doctors must be able to carry out within the framework of the law. It is important mechanisms in promoting justice for society, relying on medical and scientific knowledge for the benefit of the general public.

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