Research Article

การพัฒนาแบบจำลองคะแนนความเสี่ยงสำหรับภาวะไตวายฉับพลันในโรงพยาบาล ณ โรงพยาบาลระดับตติยภูมิแห่งหนึ่งในประเทศไทย

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บทคัดย่อ

การพัฒนาแบบจำลองคะแนนความเสี่ยงสำหรับภาวะไตวายฉับพลันในโรงพยาบาล ณ โรงพยาบาลระดับตติยภูมิแห่งหนึ่งในประเทศไทย

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ไตวายฉับพลันในโรงพยาบาลเป็นภาวะที่พบได้บ่อยในผู้ป่วยที่เข้าพักรักษาตัวในโรงพยาบาล โดยค่าการทำงานของไตจะลดลงอย่างรวดเร็วภายหลังการนอนโรงพยาบาลนานกว่า 24 ชั่วโมง ผู้ป่วยที่มีภาวะไตวายฉับพลันในโรงพยาบาลอาจเกิดผลกระทบตามมา ได้แก่ อาการแทรกซ้อนที่รุนแรง ต้องการบริการรักษาพยาบาล ระยะเวลานอนโรงพยาบาลนานขึ้น เกิดความพิการหรือเสียชีวิต ดังนั้นหากสามารถตรวจจับภาวะไตวายฉับพลันได้เร็ว ปัญหาดังกล่าวอาจได้รับการป้องกันหรือแก้ไขและสามารถลดความรุนแรงที่อาจเกิดขึ้นได้ **วัตถุประสงค์:** การศึกษานี้มีวัตถุประสงค์เพื่อพัฒนาแบบจำลองคะแนนความเสี่ยงสำหรับประเมินภาวะไตวายฉับพลันในโรงพยาบาล **วิธีดำเนินงานวิจัย:** การศึกษาแบบตามรุ่นย้อนหลังนี้ดำเนินการโดยเก็บข้อมูลจากฐานข้อมูลอิเล็กทรอนิกส์ของผู้ป่วยใน ที่มีภาวะไตวายเฉียบพลันในโรงพยาบาล (322 ราย) และผู้ป่วยในที่ไม่มีภาวะไตวาย (12,056 ราย) ณ โรงพยาบาลอุดรธานี ระหว่างวันที่ 1 เมษายน ถึง 30 กันยายน 2559 ทำการพัฒนาแบบจำลองคะแนนความเสี่ยงของภาวะไตวายฉับพลันในโรงพยาบาลจากปัจจัยเสี่ยง ประกอบไปด้วย 11 chronic medical conditions (elderly, chronic kidney disease, chronic lung disease, chronic liver disease, congestive heart failure, diabetes mellitus, hypertension, ASCVD, morbid obesity, cancer and HIV infection) และ 10 acute medical conditions (high risk operation, pH≤ 7.3, sepsis, mechanical ventilation, traumatic Brain Injury, rhabdomyolysis, anemia, hyperglycemia, decreased albumin and nephrotoxin exposure) ที่มีนัยสำคัญทางสถิติจากการวิเคราะห์การถดถอยพหุคูณ และทำการประเมินโดยใช้ผู้ป่วยทุกรายที่ครบเกณฑ์ประเมินสำหรับแบบจำลองคะแนนความเสี่ยง หาจุดตัดคะแนนที่เหมาะสมโดยใช้พื้นที่ใต้โค้งของ receiver operating characteristic curve (ROC curve) และสอบเทียบแบบจำลองโดยใช้ confusion matrix method **ผลการวิจัย:** ผลการวิเคราะห์การถดถอยพหุคูณพบว่ามี 5 ปัจจัยเสี่ยงนำมาใช้ประกอบในสมการการถดถอยพหุคูณ HA-AKI = -3.277 + [2.06(CHF)] + [1.811(ASCVD)] + [1.478(Blood pH≤7.3)] + [3.284(Sepsis)] + [1.79(Anemia)] แบบจำลองคะแนนความเสี่ยงที่สร้างขึ้นมีค่าคะแนนเต็ม 51 คะแนน ซึ่งจาก ROC curve ที่จุดตัดคะแนนที่เหมาะสม (17 คะแนน) แบบจำลองจะมีค่าพื้นที่ใต้กราฟของ ROC ดีที่สุดเท่ากับ 0.92 (95% CI: 0.90-0.95) ความไว 0.85 และความจำเพาะ 0.93 **สรุปผลการวิจัย**: แบบจำลองคะแนนความเสี่ยงนี้มีประโยชน์มากในการตรวจจับภาวะไตวายฉับพลันในโรงพยาบาลในผู้ป่วยที่มีความเสี่ยงสูง ซึ่งต้องการการดูแลอย่างใกล้ชิด

คำสำคัญ: ภาวะไตวายฉับพลันในโรงพยาบาล, แบบจำลองคะแนนความเสี่ยง

Development of Risk Score Model for Hospital-acquired Acute Kidney Injury in a Tertiary Care Hospital in Thailand

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Abstract

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Hospital-acquired acute kidney injury (HA-AKI) is a common complication in hospitalized patients and is characterized as rapidly decrease in kidney function after hospitalization over 24 hours. The consequence effect of HA-AKI might be serious complications, health-care service utilizations, longer length of stay, morbidity or mortality. Therefore, if AKI could be detected earlier, the problem would be prevented or solved, and the severity would be reduced. The aim of the study was to develop a risk score model for assessing HA-AKI. **Methods:** This retrospective cohort study was done using data from computerized hospital database belonged to inpatients with HA-AKI (322 patients) and without AKI (12,056 patients) at UdonThani Hospital during 1 April 2016 - 30 September 2016. A risk score model for HA-AKI was developed from statistically significant risk factors composed of 11 chronic medical conditions (elderly, chronic kidney disease, chronic lung disease, chronic liver disease, congestive heart failure, diabetes mellitus, hypertension, ASCVD, morbid obesity, cancer and HIV infection) and 10 acute medical conditions (high risk operation, pH$\leq$ 7.3, sepsis, mechanical ventilation, traumatic brain Injury, rhabdomyolysis, anemia, hyperglycemia, decreased albumin and nephrotoxin exposure) by multiple regression analysis and was further evaluated using all patients who met all criteria for risk score model. The optimum cut-off point and the model calibration were assessed by the area under the curve (AUC) of receiver operating characteristic (ROC) curve and confusion matrix method, respectively. **Results:** From the multiple regression analysis, 5 factors were included into multiple regression equation and presented as HA-AKI = -3.277 + [2.06(CHF)] + [1.811(ASCVD)] + [1.478(Blood pH$\leq$7.3)] + [3.284(Sepsis)] + [1.79(Anemia)]. Risk score model was developed with totally 51 points. From ROC curve of the optimum cut-off point (17 scores), this model had best yield with AUC of ROC 0.92 (95% CI: 0.90-0.95), sensitivity 0.85 and specificity 0.93. **Conclusion**: This risk score model may be very useful for detecting HA-AKI in high risk patient who need closely monitoring.

Keywords: Hospital-Acquired Acute Kidney Injury, Risk Score Model

Introduction

Acute kidney injury (AKI) is a common complication in hospitalized patients. It is characterized as rapidly decrease in kidney function during hospitalization that may occur within first 24 h (community-acquired AKI, CA-AKI) or after first 24 h (hospital-acquired AKI, HA-AKI). (Dager and Halilovic, 2015) In general, the incidence of AKI was estimated to 2-20% of hospitalized patients and the mortality rate was about 40%. (Jade *et al.*, 2017; Nie *et al.*, 2017; Yang *et al.*, 2015; Pan *et al.*, 2016) The incidence and mortality rate of AKI might increase up to 20-60% and 30-90%, respectively, in critical-ill patients. The prevalence of CA-AKI is usually higher than HA-AKI but the mortality rate is vice versa. (Wonnacott *et al*, 2014) The consequent effects of AKI might be serious complications, health-care service utilizations (i.e., mechanical ventilation, renal replacement therapy), longer length of stay, morbidity or mortality. Furthermore, chronic kidney disease (CKD) may develop in some patients. (Meier *et al.*, 2011; Chertow *et al.*, 2005) Diagnosis of AKI is complicate, therefore, many agencies have established diagnostic criteria such as Risk, Injury, Failure, Loss of Kidney Function and End Stage Renal Failure (RIFLE) criteria (Bellomo *et al.*, 2004), Acute Kidney Injury Network (AKIN) criteria (Mehta *et al.*, 2007) and Kidney Disease: Improving Global Outcome (KDIGO) criteria. (John *et al.*, 2012)

There are many risk factors related to AKI including advanced age, pre-exist chronic kidney injury, chronic lung disease, chronic liver disease, heart failure, high blood pressure, diabetes mellitus, coronary artery disease, severe infection or sepsis, cancer, high risk operation, use of mechanical ventilation, anemia, low blood pH, hypoalbuminemia, hyperglycemia, morbid obesity, rhabdomyolysis and nephrotoxin exposure. (Nie *et al.*, 2017; Wonnacott *et al.*, 2014) Therefore, early recognition of risk to AKI may be useful for healthcare professionals in risk factor prevention and/or correction. Previous AKI risk assessment was developed using specific factors including underlying disease, comorbidity, abnormal laboratory value, acute medical condition or biomarkers of kidney injury which were not suitable for use in Thailand. (Malhotra *et al.*, 2017) Some variables are not routinely tested in most of hospitals in Thailand such as neutrophil gelatinase–associated lipocalin (NGAL), kidney injury molecule 1 (KIM-1), cystatin C and IL-18 and some variables are directly related to HA-AKI such as volume depletion, dehydration or bleeding. Therefore, HA-AKI risk score model was developed for using in our tertiary care hospital.

Methods

This retrospective cohort study was performed using data from computerized hospital database. The study was approved by Ethic Committee of Human Research, KhonKaen University (HE602359) and UdonThani Hospital (No. 22/2561)

Study population

Adult patients with age $\geq$ 18 years who were admitted to UdonThani Hospital at inpatient department during April to September 2016 were recruited into the study. Patients with AKI diagnosis by ICD-10 code (N17.0, N17.1, N17.2, N17.8, N17.9) after 24 hours of hospitalization were included into the study and classified as HA-AKI group. Patients without AKI diagnosis were included into the study and classified as comparator or non-AKI group. Exclusion criteria were patients who underwent renal replacement therapy by hemodialysis, peritoneal dialysis and kidney transplantation. Patients with AKI diagnosis on admission day or less than 24 hours of hospitalization (CA-AKI) were also excluded.

Sample size calculation

The formula of Taro Yamane (1967) $n = N/1+Ne^2$, when n = calculated sample size, N = number of known populations, e = tolerance value (0.05). In 2016, 2,749 patients with AKI were diagnosed at UdonThani Hospital. Previous study by Chien-Ning Hsu and his college reported that the ratio of HA-AKI: CA-AKI in hospitalized patients

was about 1:2. Therefore, 900 patients with HA-AKI was predicted in 2016 at UdonThani Hospital and 276 patients with HA-AKI were recruited into the study. The number of samples was rounded to totally 300 patients for substituting missing data or exclusion. All patients with or without AKI, had complete laboratory data and admitted in the same period were used in the validation process.

Data collection

Information of eligible patients were collected from electronic database composed of patient demography (age, sex, weight, and height), laboratory values (serum creatinine, blood pH), medical conditions or diseases, and medications. These data were assumed to be the risk factors for acute kidney injury, which were divided into 11 chronic medical conditions and 10 acute medical conditions. Chronic medical conditions composed of elderly ($\geq$65yr), CKD stage 3-5, chronic liver disease, diabetes mellitus (DM), hypertension (HT), heart failure (HF), arteriosclerotic coronary artery disease (ASCVD), morbid obesity (body mass index or BMI >30.0 kg/m^2), chronic lung disease, active cancer, human immunodeficiency virus infection (HIV). Acute medical conditions composed of high-risk surgery (cardiac, aortic and hepatobiliary surgery), blood pH $\leq$7.3, sepsis, mechanical ventilation, traumatic brain Injury, rhabdomyolysis, anemia, hyperglycemia, hypoalbuminemia and nephrotoxin exposure (amphotericin B, aminoglycosides, radio contrast, chemotherapy, anti-retroviral drugs, non-steroidal anti-inflammatory drugs except aspirin, angiotensin converting enzyme inhibitors (ACEIs), angiotensin receptor blockers (ARBs) and diuretics). Date of discharge and discharge status were used for calculating length of hospital stay and mortality rate, respectively.

Data and statistical analysis

Data from patients with HA-AKI and patients without AKI were summarized and compared; then, univariate and multivariate analyses were used to find the significant risk factors. Relationship between HA-AKI and medical risk factors either chronic or acute medical condition were assessed and then were used to develop the HA-AKI risk score model. The Confusion Matrix method (2x2 table) was compared with standard tool (KDIGO2012) to calculate the sensitivity, specificity, accuracy, etc. in validation process. A confusion matrix is formed from the four outcomes produced as a result of binary classification. A binary classifier predicts all data instances of risk score model and standard tool as either positive or negative. This classification (or prediction) produces four outcomes – true positive, true negative, false positive and false negative. The appropriate cut-off point of the model was examined by calculating the area under curve (AUC) after creating the receiver's characteristic (ROC) curve.

Statistical analysis was carried out using STATA software, version 10.0. Data were analyzed with the confidence interval at 95% (α = 0.05) and the significance level at p-value = 0.05. Descriptive statistics for continuous data were expressed as mean $\pm$ SD or median (IQR) and the difference between groups were analyzed by unpaired t-test. Categorical variables were expressed as absolute (n) and relative (%) frequency and the difference between groups were analyzed by Chi-square test. The relationship between the risk factors to HA-AKI were analyzed by binary logistic regression and multiple regression analysis.

Results

Patients' characteristics and medical conditions

A total of 13,478 patients were hospitalized during the study period. AKI was diagnosed in 1,422 patients but 1,100 patients with CA-AKI (7.97%) were excluded, meanwhile, 322 patients with HA-AKI (2.33%) and 12,056 patients without AKI were included into this study. Patients with HA-AKI aged between 18-99 years with average age 60 years and women were predominant (55.81%). The average onset of HA-AKI was 2 days. The mortality rate of patients with HA-AKI was higher than patients without AKI, 29.5% and 8.3%, respectively, as shown in Table 1.

Development of a risk score model for HA-AKI

All 21 medical conditions were analyzed and considered to be the risk factors to HA-AKI with statistical significance except for morbid obesity as shown in Table 1. However, risk factors with statistical significance greater than 0.05 were removed in binary logistic regression by backward elimination method until all of risk factor had p-value lower than 0.05. (Table 2). Final model, 5 factors were included into the formula for predicting HA-AKI = -3.277 + [2.06(CHF)] + [1.811(ASCVD)] + [1.478(Blood pH≤7.3)] + [3.284(Sepsis)] + [1.79(Anemia)]. Finally, B-coefficient of each risk factors were converted to integer point in the risk score model with totally 25.5 points as shown in Table 3.

In validation process, there were 483 patients in 6-month periods who had complete data of 5 risk factors as shown in Table 4. Risk score model was performed and then, tested with 483 patients who met all criteria; 229 patients with HA-AKI and 254 patients without AKI and the test values were presented in Table 5. The optimum cut-off points of HA-AKI risk score model was greater than or equal to 17, that presented AUC of ROC curve 0.92 (0.90-0.95), sensitivity equal 0.85, and specificity 0.93. If the cut-off points at 16 points is selected, the sensitivity will increase to 0.91 but the specificity will decrease to 0.83. If the cut-off point is increased to 18 points, the sensitivity will reduce to 0.83 and the specificity will increase to 0.93. Therefore, using the cut-off at 17 points gives the optimal sensitivity and specificity value. ROC curve could be plotted as shown in Figure 1.

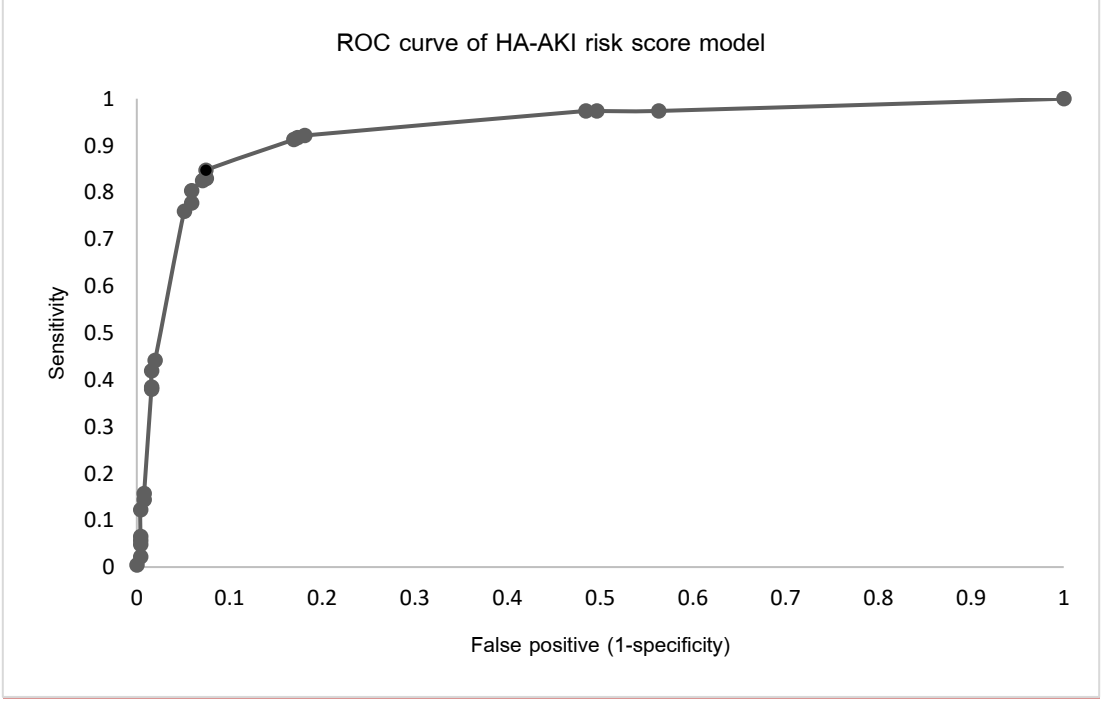

Figure 1 ROC curve of HA-AKI score

Table 1 Patients' demography and characteristics

Factors	Patients with HA-AKI (n = 322)(%)	Patients without AKI (n = 12,056)(%)	P-value	Crude OR (95%CI)
Demography				
Age (mean ± SD)	60±16.1 yr	52±16.8 yr	<0.001[a]	
Male : Female	210 (65.2):112 (34.9)	5,260 (43.6):6,796 (56.2)	<0.001[b]	
BMI (mean ± SD)	22.9±5.5 kg/m^2	23.5±4.7 kg/m^2	0.079[a]	
Hospitalization data				
Median AKI onset (range)	2 days (1-26 days)	-	-	
Total length of stay	4,185 patient-day	60,479 patient-day	-	
Average length of stay	13 day/patients	4.89 day/patients		
Death	95 (29.5)	1028 (8.3)	<0.001[b]	
Chronic medical conditions				
Elderly (>65 yr)	143 (44.41)	3,095 (25.67)	<0.001[b]	2.31 (1.84-2.91)
Chronic kidney disease	74 (22.98)	886 (7.35)	<0.001[b]	3.76 (2.84-4.94)
Chronic lung disease	29 (9.01)	316 (2.62)	<0.001[b]	3.68 (2.47-5.47)
Chronic liver disease	30 (9.32)	161 (1.34)	<0.001[b]	7.59 (5.05-11.40)
Congestive heart failure	73 (22.67)	77 (0.64)	<0.001[b]	45.61 (32.34-64.33)
Diabetes mellitus	104 (32.30)	1,175 (9.75)	<0.001[b]	4.42 (3.47-5.62)
Hypertension	130 (40.37)	1,218 (10.10)	<0.001[b]	6.02 (4.79-7.59)
ASCVD[e]	53 (16.46)	80 (0.66)	<0.001[b]	29.49 (20.42-42.60)
Morbid obesity[c]	22/267 (8.24)	738/10,658 (6.92)	0.404[b]	1.46 (1.13-1.89)
Cancer	36 (11.18)	736 (6.10)	<0.001[b]	1.94 (1.36-2.76)
HIV infection[f]	13 (4.04)	12 (0.10)	<0.001[b]	42.23(19.11-93.29)
Acute medical condition				
High risk operation	34 (10.56)	281 (2.33)	<0.001[b]	4.95 (3.40-7.19)
pH ≤ 7.3[c]	87/230 (37.83)	36/254 (14.17)	<0.001[b]	123.61 (82.09-186.13)
Sepsis	221 (68.63)	156 (1.29)	<0.001[b]	166.91 (125.71-121.62)
Mechanical ventilation	170 (52.80)	391 (3.24)	<0.001[b]	33.37 (26.22-42.45)
Traumatic Brain Injury	4 (1.24)	19 (0.16)	<0.001[b]	7.97 (2.70-23.56)
Rhabdomyolysis	15 (4.66)	7 (0.06)	<0.001[b]	84.10 (34.05-207.74)
Anemia	280 (86.96)	1,971 (16.35)	<0.001[b]	34.11 (24.58-47.35)
Hyperglycemia[c]	107/277 (40.07)	518/2,040 (25.39)	<0.001[b]	0.15 (0.12-0.18)
Decreased albumin[c]	203/292 (69.52)	1,476/4,548 (32.45)	<0.001[b]	12.23 (9.69-15.43)
Nephrotoxin exposure[c, d]	158/312 (50.64)	2,358 (19.56)	<0.001[b]	4.22 (3.36-5.29)

a = unpaired t-test

b = Chi square-test

c = for patient with data available

[d] Nephrotoxin exposure = Amphotericin B, aminoglycosides, radio contrast, chemotherapy, anti-retroviral drugs, non-steroidal anti-inflammatory drugs (except aspirin), renin angiotensin aldosterone system blocker, diuretics

[e] ASCVD = Atherosclerotic coronary vascular disease

[f] HIV = Human immunodeficiency virus

Table 2 Binary regression and multiple regression analysis of HA-AKI risk factors

Risk factor	Binary regression analysis			Backward elimination		
	B-Coefficient	Adjusted OR (95%CI)	P-value	B-Coefficient	Adjusted OR (95%CI)	P-value
Chronic medical condition						
Elderly	-0.128	0.88 (0.37-2.09)	0.771	-	-	-
Chronic kidney disease	-0.417	0.66 (0.25-1.74)	0.401	-	-	-
Chronic lung disease	-0.511	0.60 (0.14-2.65)	0.500	-	-	-
Chronic liver disease	1.898	6.67 (0.73-61.02)	0.093	-	-	-
Congestive heart failure	1.964	7.13 (1.95-26.03)	0.003*	2.060	7.85 (2.98-20.67)	<0.001*
Diabetes mellitus	-0.579	0.56 (0.20-1.58)	0.273	-	-	-
Hypertension	0.833	2.30 (0.87-6.06)	0.092	-	-	-
ASCVD	2.059	7.84 (1.44-42.75)	0.017*	1.811	6.12 (2.19-17.06)	0.001*
Cancer	-	-	-	-	-	-
HIV infection	0.771	2.16 (0.66-7.11)	0.204	-	-	-
Acute medical condition						
High risk operation	0.125	1.13 (0.27-4.82)	0.865	-	-	-
pH $\leq$ 7.3	2.110	8.25 (2.69-25.28)	<0.001*	1.478	4.39 (2.30-8.37)	<0.001*
Sepsis	0.939	51.35 (18.16-145.17)	<0.001*	3.284	26.69 (14.49-49.18)	<0.001*
Mechanical ventilation	-0.312	0.73 (0.29-1.82)	0.502	-	-	-
Traumatic Brain Injury	-	-	-	-	-	-
Rhabdomyolysis	-	-	-	-	-	-
Anemia*	1.599	4.95 (1.83-13.35)	0.002*	1.790	5.99 (3.25-11.06)	<0.001*
Hyperglycemia	0.365	1.44 (0.55-3.75)	0.455	-	-	-
Decreased albumin	-0.124	0.88 (0.35-2.26)	0.797	-	-	-
Nephrotoxin exposure	-0.599	0.55 (0.23-1.34)	0.187	-	-	-
constant	-2.701			-3.277		

* Statistically significant

Table 3 Risk assessment model of hospital acquired acute kidney injury

Risk factor	Risk score	Assessment
Chronic medical condition		
• Congestive heart failure	11	_____
• Atherosclerotic coronary vascular disease	8	_____
Acute medical condition		
• Blood pH ≤ 7.3	7	_____
• Sepsis	16	_____
• Anemia	9	_____
Total	**51**	_____

If total score ≥ 17, HA-AKI may occur

Table 4 Patients' demography and characteristics in risk score model validation

Risk factors	Number of case (%)	
	HA-AKI (n = 229)	No-AKI (n = 254)
Gender		
Male	146 (63.76)	149 (58.66)
Female	83 (36.24)	105 (41.34)
Congestive heart failure	51 (22.27)	9 (3.54)
Atherosclerotic coronary vascular disease	35 (15.28)	8 (3.15)
Blood pH< 7.3	90 (39.30)	37 (14.57)
Sepsis	172 (75.11)	23 (9.06)
Anemia	201 (87.78)	107 (42.13)

Table 5 Validation of HA-AKI risk score model

Cutoff	Sensitivity	Specificity	Accuracy	PPV	NPV	LR+	LR-	Prevalence	OLR	PP
0	1.00	0.00	0.47	0.47	0.00	1.00	0.00	0.47	0.00	0.47
7	0.97	0.44	0.69	0.61	0.95	1.73	0.06	0.47	28.85	0.61
8	0.97	0.50	0.73	0.64	0.96	1.96	0.05	0.47	37.76	0.64
9	0.97	0.52	0.73	0.64	0.96	2.01	0.05	0.47	39.58	0.64
11	0.92	0.82	0.87	0.82	0.92	5.09	0.10	0.47	53.00	0.82
12	0.92	0.83	0.87	0.83	0.92	5.29	0.10	0.47	52.75	0.83
16	0.91	0.83	0.87	0.83	0.91	5.39	0.11	0.47	51.28	0.83
17	0.85	0.93	0.89	0.91	0.87	11.33	0.17	0.47	68.56	0.91
18	0.83	0.93	0.88	0.91	0.86	11.09	0.18	0.47	60.26	0.91
20	0.83	0.93	0.88	0.91	0.86	11.65	0.19	0.47	61.95	0.91
23	0.80	0.94	0.88	0.92	0.84	13.61	0.21	0.47	65.15	0.92
24	0.78	0.94	0.86	0.92	0.82	13.16	0.24	0.47	55.61	0.92
25	0.76	0.95	0.86	0.93	0.81	14.85	0.25	0.47	58.65	0.93

Table 5 Validation of HA-AKI risk score model *(Cont.)*

Cutoff	Sensitivity	Specificity	Accuracy	PPV	NPV	LR+	LR-	Prevalence	OLR	PP
27	0.44	0.98	0.72	0.95	0.66	22.41	0.57	0.47	39.30	0.95
28	0.42	0.98	0.72	0.96	0.65	26.62	0.59	0.47	45.11	0.96
31	0.38	0.98	0.70	0.96	0.64	24.40	0.63	0.47	39.01	0.96
32	0.38	0.98	0.70	0.96	0.64	24.12	0.63	0.47	38.29	0.96
33	0.16	0.99	0.60	0.95	0.57	19.97	0.85	0.47	23.50	0.95
35	0.14	0.99	0.59	0.94	0.56	18.30	0.86	0.47	21.21	0.94
36	0.12	1.00	0.58	0.97	0.56	31.06	0.88	0.47	35.24	0.97
40	0.07	1.00	0.55	0.94	0.54	16.64	0.94	0.47	17.73	0.94
42	0.06	1.00	0.55	0.93	0.54	14.42	0.95	0.47	15.23	0.93
43	0.05	1.00	0.55	0.92	0.54	12.20	0.96	0.47	12.77	0.92
44	0.02	1.00	0.53	0.83	0.53	5.55	0.98	0.47	5.65	0.83
51	0.00	1.00	0.53	1.00	0.53	0.00	1.00	0.47	0.00	1.00

PPV = positive predictive value, NPV = negative predictive value, LR+ = likelihood ratios for positive test,
LR- = likelihood ratios for negative test, OLR=odds-likelihood ratios, PP=post-test probability

Discussion

The incidence rate of AKI in hospitalized patients at UdonThani Hospital in 6-month period was 10.3%; CA-AKI 7.97% and HA-AKI 2.33%. The ratio of CA-AKI: HA-AKI was 3.42: 1 which was within the ratio between 1: 1 to 4:1 in previous reports. (Treamtrakanpon and Khongkha, 2016; Vikrant *et al.*, 2018) The incidence of AKI in the present study was higher than 2.21% in 1-year period at Chaopraya Abhaibhubejhr Hospital, a tertiary care hospital with 500-bed in central region of Thailand. This may result from difference size of hospital and workload such as more severe medical conditions of patients in this study since UdonThani Hospital is a super tertiary care hospital and medical center with 1000-bed in northeast region of Thailand. The incidence of HA-AKI in UdonThani Hospital was higher than 0.78% in the previous study in the multicenter study in Taiwan (Hsu *et al.*, 2016), which defined AKI by RIFLE criteria. RIFLE criteria had lower sensitivity and specificity than AKIN and KDIGO2012 criteria so that some AKI patients could not be detected in the previous study.(Luo *et al.*, 2014)

Male patients with HA-AKI was twice as many as female patients which contrasted to previous study in Thailand and worldwide.(Hsu *et al.*, 2016; Inokuchi *et al.*, 2017) However, previous study also reported that the number of dialysis required AKI in male patients were twice as many as female patients (OR 2.19, 90% CI: 2.15-2.22, p < 0.0001) (Neugarten *et al.*, 2018) which was similar to the number of dialysis required AKI in 20 male and 9 female patients in this study. Moreover, patients with 6 complete data of risk factors in model calibration were male (n = 295) rather than female (n =188). Average age of patients with HA-AKI from the studies in Europe and America were higher than both studies in Asia and this study. This may result from the better policy and system of health care in developed countries that supported the better health and longer live of people so that AKI may be occurred in patients with older age than in developing countries. However, the onset of HA-AKI about 2 days in this study was similar to previous studies in US. (Goswami *et al.*, 2016; Holmes *et al.*,2016; Inokuchi *et al.*, 2017; Mohammed *et al.*, 2018; Susantitaphong *et al.*, 2013)

Five factors selected to this model were similar to previous study. Sepsis was the risk factor with the highest

predictive value for HA-AKI in present study similar to previous study. (Bagshaw *et al.*, 2008; Koyner *et al.*, 2016; Suh *et al.*, 2013;) When the host immune systems fight with the pathogen invading into the body, inflammation will occur and cause damage or obstruction of the blood vessel of many organ included kidney. (Poston and Koyner, 2019) Inflammatory process also occur in case of decrease blood pH <7.3, the second rank high predictive value, by increasing the secretion of biochemical substance and then decrease blood flow to the kidney. On the other hand, nephrotoxin exposure was found to be a risk factor with high positive predictive value in previous study (Hu *et al.*, 2017) but was found to be a risk factor with low negative predictive value in present study. The different result may be due to lack of medical database network of all hospitals in Thailand and incomplete medical reconciliation system. Therefore, many patients who did not have past medical history were excluded in the present study, resulting in the factor of nephrotoxin exposure shown different result. HA-AKI risk score model with 5 risk factors in this study had a full score of 51 points, but the optimum cut-off point was greater than or equal to 17 points, with a good sensitivity 0.85 and specificity 0.93 which was better than sensitivity 0.91 and specificity 0.83 for the cut-off at 16 points or sensitivity 0.83 and specificity 0.93 for the cut-off at 18 points. AUC of ROC curve was 0.92 (0.90-0.95) which was relatively high and could confirm the appropriateness of the model.

There are many strengths of this study. First, the KDIGO2012 diagnostic criteria were used which is better than AKI assessment using SCr alone in previous studies. Second, the risk score model in present study is specific to HA-AKI which causes high mortality rate in hospitalized patient. Finally, the risk score model had 2 chronic medical conditions and 3 acute medical conditions which are easy to assess in all hospitalized patients. We sincerely hope that this HA-AKI risk score model may be useful for healthcare professional to assess the hospitalized patients and plan to reduce the incidence and severity of HA-AKI in the hospital. When patients who at risk of HA-AKI is detected, healthcare professional should concern AKI prevention and management such as supplementation of adequate water fluid and hasten to solve medical conditions. In addition, avoiding of nephrotoxin exposure and dosage adjustment of medicine must be recommended in accordance with renal function to decrease the harm to patients. (Mas *et al.*, 2017)

Conclusion

The incidence of HA-AKI is relatively low, but mortality rate was high. There were 5 risk factors in risk score model included CHF, ASCVD, blood pH≤ 7.3, sepsis and anemia. The optimum cut-off point is 17 scores which presents sensitivity 0.85, specificity 0.93 and accuracy 0.89. This risk score model may be useful for health care professional to detect high risk patient who need closely monitoring.

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Conflict of interest

This study had financial support by grant for academic purpose, there was no bias in terms of conflict of interest.

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