Original Contribution

Predictors of early clinical deterioration after acute ischemic stroke

American Journal of Emergency Medicine (2011) 29, 577-581

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Introduction

- Among stroke patients, 20% to 40% will experience early deterioration in condition after hospital admission.
- Early admission to a stroke unit
- In previous reports, many predictors of early deterioration after ischemic stroke have been proposed and studied, yet the results remain controversial.

Introduction

- Overall status and stroke severity:
1. initial NIHSS score;
2. early CT findings of stroke severity;
3. changes in cerebral blood flow affecting the ischemic penumbra(PET & single-photon emission CT)…
- Laboratory tests:
1. coagulation markers(fibrinogen, Ddimers)
2. inflammatory markers(↑ IL-6, ↓ IL-10)
3. serum glucose, hematocrit

Introduction

- Physiologic parameters:
1. blood pressure
2. BT
- Medical history
1. DM
2. Atherosclerosis
3. chronic heart disease
- Different stroke subtypes

Introduction

- A predictor of early deterioration that is equally applicable to all stroke subtypes is needed
- Identify risk factors for early deterioration after stroke (regardless of stroke subtype)
- Determine predictors
1. Readily assessed in an ED setting
2. identify high-risk stroke patients

Methods

- Acute ischemic stroke
- Consecutive patients admitted to the Chia-Yi Chang Gung Memorial Hospital
- July 2007 to June 2008
- Patients were excluded
  - previous acute ischemic stroke
  - neurologic symptoms more than 12 hours
  - hemorrhagic stroke
  - required fibrinolytic therapy
  - TIA

Methods- data collection

- Sex
- symptoms and signs
- Glasgow Coma Scale (GCS)
- Past & personal history
- stroke localization
- Electrocardiogram
- arterial blood pressure (ED & Q8H *3d)
- blood glucose,HbA1c
- complete blood count
- C-reactive protein , D-dimer
- Blood urea nitrogen (BUN); creatinine (Cr); BUN/Cr,AST/ALP, albumin，TG,T-cho,LDL
- brain CT scan within 6 hours

Stroke-in-evolution

- Each patient's neurologic condition was assessed by a neurologist from the stroke team who was blinded to all other patient data.
- Stroke severity was assessed using the NIHSS score.
- Patients with early deterioration in condition were defined as having stroke-in-evolution (SIE).
- Cutoff point : HIHSS score increase ≥3

Methods

- The study end point was patient outcome on day 3 as measured by the NIHSS
- The patients were divided into 2 groups for data analysis
  - stroke-in-evolution
  - Without stroke-in-evolution.
- Analysis was performed to identify potential risk factors for SIE.
  - BUN/Cr more than 15(prerenal azotemia and dehydration)

Statistical analysis

- Continuous data are expressed as mean ± SD.
- Categorical data are expressed as frequencies and percentage.
- Demographic characteristics were compared using Student t test or χ 2 test.
- Age, sex, and variables found to be associated with SIE by univariate logistic regression analysis were entered into multivariate logistic regression models.

Results

Table 1 Demographic and clinical characteristics of the 196 study patients

Variables (missing no)	Non-SIE (n = 166)	SIE (n = 30)	*P*
Age[a] (y) (1)	70.3 ± 10.3	72.2 ± 11.0	.373
Male[b]	106 (63.9)	20 (66.7)	.767
D-Dimer >1000[b]	57 (35.2)	16 (53.3)	.060
ECG-af[b]	40 (24.1)	8 (26.7)	.763
Systolic blood pressure[a] (3)	167.3 ± 36.9	171.2 ± 31.5	.584
Diastolic blood pressure[a] (3)	90.7 ± 17.7	97.3 ± 25.6	.188
Blood sugar[a] (3)	165.5 ± 87.5	174.8 ± 85.9	.594
AST[a] (66)	28.9 ± 25.4	30.9 ± 33.1	.749
ALT[a] (5)	27.1 ± 17.7	29.6 ± 20.1	.495
BUN[a] (50)	16.1 ± 10.5	13.4 ± 9.3	.644
Cr[a]	1.1 ± 0.8	1.1 ± 0.6	.969
BUN/Cr >15[b] (50)	37 (31.1)	16 (59.3)	.006*

Table 1 Demographic and clinical characteristics of the 196 study patients

Variables (missing no)	Non-SIE (n = 166)	SIE (n = 30)	*P*
TG[a] (41)	119.6 ± 61.5	123.7 ± 91.0	.825
Total Chol[a] (31)	179.2 ± 40.8	185.9 ± 34.9	.440
Uric acid[a] (56)	5.5 ± 1.8	5.8 ± 2.0	.386
Albumin[a] (1)	4.4 ± 3.2	4.0 ± 0.5	.118
WBC[a]	7.8 ± 2.8	7.8 ± 2.6	.903
Hgb[a]	13.6 ± 1.7	12.9 ± 2.0	.990
PLT[a] (1)	206.7 ± 65.2	208.8 ± 79.8	.878
SEG[a] (2)	0.6 ± 0.1	0.7 ± 0.1	.795
WBC * (SEG + Band)[a] (4)	5.3 ± 2.5	5.3 ± 2.4	.876
LDL[a] (38)	112.5 ± 31.6	121.4 ± 30.6	.202
HbAlc[a] (95)	0.07 ± 0.02	0.08 ± 0.03	.559
OCSP[a] (40)	1.9 ± 1.3	2.2 ± 1.4	.286

Table 2 NIHSS and GCS recorded on ED admission of the 196 study patients

Variables	Non-SIE (n = 166)	SIE (n = 30)	*P*
NIHSS	7.3 ± 6.6	9.6 ± 7.2	.093
<12	128 (77.6)	17 (58.6)	.030 *
≥12	37 (22.4)	12 (41.4)	
GCS	14.1 ± 1.9	13.1 ± 2.7	.012 *
>12	139 (83.7)	20 (66.7)	.028 *
≤12	27 (16.3)	10 (33.3)	

Continuous data expressed as mean ± SD, and categorical data expressed as %.
* Statistically significant at $P < .05$.

Table 3 Univariate logistic regression analysis for possible factors associated with SIE

Variables	OR *	95% CI	*P*
Age (per year)	1.02	0.98-1.06	.371
Sex			
Female	Reference	–	
Male	1.32	0.50-2.58	.768
d-Dimer			
≤1	Reference	–	
>1	2.11	0.96-4.62	.064
BUN/Cr			
≤15	Reference	–	
>15	3.22	1.36-7.62	.008 *
GCS			
>12	Reference	–	
≤12	2.57	1.09-6.11	.032 *
NIHSS			
<12	Reference	–	
≥12	2.44	1.07-5.57	.034 *

Tested with univariate logistic regression analysis and presented with OR and 95% CI.
* Statistically significant at $P < .05$.

Table 4 Multivariate logistic regression analysis for possible factors associated with SIE

Variables	OR *	95% CI	*P*
Age (per year)	1.02	0.98-1.07	.399
Sex			
Female	Reference	–	
Male	1.37	0.52-3.58	.520
BUN/Cr			
≤15	Reference	–	
>15	3.41	1.38-8.46	.008 *
NIHSS			
<12	Reference	–	
≥12	1.29	0.50-3.37	.601

Tested with multivariate logistic regression analysis and presented with OR and 95% CI.
* Statistically significant at $P < .05$.

Discussion- BUN/Cr ratio

- BUN/Cr ratio at admission was an independent predictive factor for early deterioration after stroke
- Chronic heart failure(Cardiovascular disease V.S stroke)
- BUN levels may be broadly indicative of underlying cardiovascular-renal-cerebrovascular susceptibilities
- renal insufficiency may lead to neurologic worsening in stroke patients

Discussion- BUN/Cr ratio

- Dehydration→a predisposition for venous thromboembolism.
- intervention for such patients should be the maintenance of proper hydration

Limitation

- Sample size
- Choice of NIHSS and GCS measure cutoff scores
- Day-to-day BUN/Cr ratio

Original Contribution

Risk stratification omogram for nephropathy after abdominal contrast-enhanced computed tomography

American Journal of Emergency Medicine (2011) 29, 412-417

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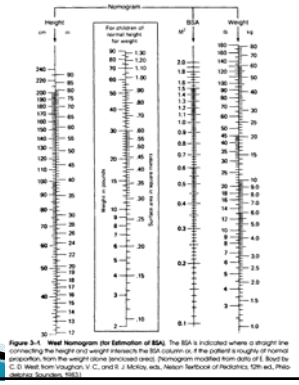
Introduction

- Contrast-induced nephropathy (CIN) is the third leading cause of hospital-acquired acute renal insufficiency and is associated with an increased mortality
- abdominal contrast-enhanced computed tomography(A-CECT) has been increasingly used in ED
- older with more comorbid conditions
- insufficient volume expansion

Introduction

- There are insufficient data reporting CIN after intravenous contrast material administration especially in emergency patients.
- Develop risk stratification nomogram for nephropathy in patients receiving emergency A-CECT using clinical variables available before the procedure.

nomogram



Methods

- Retrospective medical record review
- Electronic medical record system
- Received A-CECT in the ED between August 2003 and January 2007.
- A total of 5421 patients were identified. Excluding
  - 25 patients without a SCr before ACECT
  - 4606 patients without a postcontrast SCr
  - 5 patients undergoing renal replacement therapy
  - 35 patients younger than 15 years

750 patients

Measurements

- Demographics (age, sex)
- Underlying diseases (diabetes, hypertension, and malignancy)
- Type and volume of intravenous radiographic contrast material, baseline vital signs, and laboratory results
- Nonionic, low-osmolar contrast material(Ultravist or Iomeron) using similar volumes and infusion rates (2 mL/kg at an infusion rate of 3 mL/s).

Measurements

- Initial SCr levels and all SCr levels over the subsequent 3 days were recorded.
- Within 24 hours before A-CECT was defined as the initial SCr.
- CIN was defined as either an absolute increase of 0.5 mg/dL or a relative increase of 25% or more in the SCr from baseline.
- follow-up SCr was required to be at least 1.5

Statistical analysis

- Continuous variables were expressed as means with SDs
- categorical data were presented as the percent frequency of occurrence.
- A 2-tailed Student t test was used to compare continuous variables, and the $\chi 2$ test or Fisher exact test was used to compare binomial variables.

Statistical analysis-derive prediction nomogram

- careful univariable analysis
- selecting minimum candidate variables with significance in univariate analysis
- Because the number of patients who fulfilled nephropathy criteria was only 34 the number of variables included in the model was limited up to 4 to avoid overfitting.
- Multivariable logistic models using these candidate variables and chose 1 model with best fit determined by Bayesian information criterion

Statistical analysis-derive

- The performance of the model was tested with respect to disc rimination and calibration.
- Discrimination was quantified with areas under the receiver operating characteristics curve (AUCs).
- Calibration was tested with graphical representations of the relationship between the observed probabilities and the predicted probabilities (calibration curves)

Results

Table 1 Patient characteristics by development of nephropathy (N = 750)

	Nephropathy (+) (n = 34)	Nephropathy (−) (n = 716)	*P*
Age (y)	69.9 ± 14.1	55.2 ± 19.1	<.001
Male sex	22 (64.7%)	396 (55.3%)	.281
Underlying diseases			
DM	8 (23.5%)	79 (11.0%)	.048 [a]
HTN	11 (32.4%)	147 (20.5%)	.099
Malignancy	8 (23.5%)	116 (16.2%)	.261
Contrast media			
Ultravist	32 (94.1%)	658 (91.9%)	1.000 [a]
Volume (gI) [b]	50.4 ± 8.6	48.3 ± 9.2	.193
Baseline vital signs			
Mean BP (mm Hg)	88.0 ± 19.4	95.1 ± 16.9	.018
HR (beats/min)	98.0 ± 29.1	88.3 ± 18.6	.062
RR (breaths/min)	21.2 ± 3.5	20.3 ± 2.8	.178
BT (°C)	36.8 ± 1.0	36.9 ± 0.9	.570
Basal SCr (mg/dL)	1.7 ± 1.1	1.1 ± 0.5	.002

Results

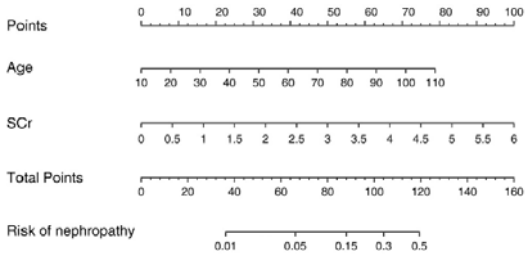
Table 2 Logistic regression analysis for estimating the risk of nephropathy

	Unadjusted OR [a]	*P*	Adjusted OR [b]	*P*
Age (y)				
1 increment	1.05 (1.03-1.08)	<.001	1.04 (1.02-1.07)	.001
Basal SCr (mg/dL)				
1 increment	2.89 (1.95-4.29)	<.001	2.51 (1.67-3.78)	<.001

OR indicates odds ratio.

[a] Unadjusted OR was derived from univariate logistic regression analysis.

[b] Adjusted OR was derived from multivariate logistic regression analysis with variables including age and basal SCr.



Internal validation

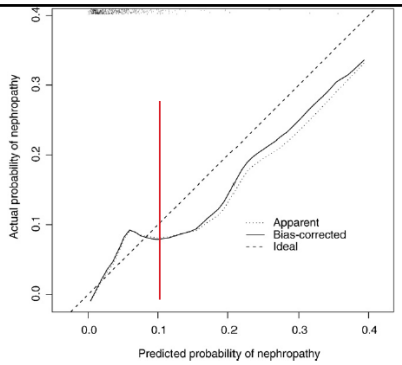


Fig. 2 Predictive accuracy of the nomogram to predict nephropathy after receiving emergency A-CECT. Predicted and observed nephropathy rates were plotted, and logistic calibration was performed using bootstrapping methods (200 repetitions).

Internal validation

- The model had a tendency to overestimate when the predicted probability was over 0.10.
- The AUC of the final prediction model in the training set was 0.794 (95% confidence interval; 0.734–0.854) and the corrected AUC with bootstrapping methods using 200 repetitions was 0.794 (95% confidence interval; 0.737–0.851).

Area under the curve(AUC)

AUC=0.5	幾乎沒有判別力 (no discrimination)
0.7≦AUC<0.8	可接受的判別力 (acceptable discrimination)
0.8≦AUC<0.9	好的判別力 (excellent discrimination)
AUC ≧0.9	非常好的判別力 (outstanding discrimination)

ROC curve

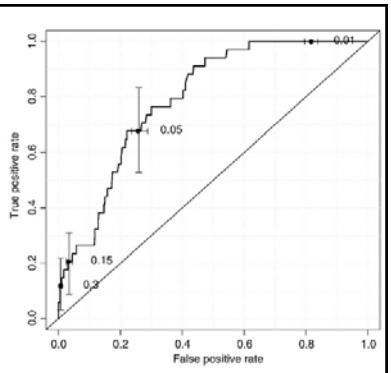


Fig. 3 The receiver operating characteristics curves of the nomogram in the training sets and bootstrapped 95% confidence intervals were plotted at cutoff values of 0.01, 0.05, 0.15, and 0.3 (200 repetitions).

Actual distribution of nephropathy

Table 3 Predicted probability versus actual distribution of nephropathy

	Predicted probability			
	<1%, very low	1%-5%, low	5%-15%, moderate	15%<, high
Actual distribution (nephropathy/total)	0/130 (0%)	11/411 (2.68%)	16/178 (8.99%)	7/31 (22.58%)

Diagnostic performances

Table 4 Diagnostic performances at each level of predicted probabilities[a]

	Sensitivity	Specificity	Positive LR	Negative LR
1%	100 (89.7-100)	18.2 (15.4-21.2)	1.22 (1.18-1.26)	NA
5%	67.6 (49.5-82.6)	74.0 (70.6-77.2)	2.60 (2.00-3.39)	0.44 (0.27-0.71)
15%	20.6 (8.7-37.9)	96.6 (95.1-97.8)	6.14 (2.85-13.2)	0.82 (0.69-0.98)

LR indicates likelihood ratio; NA, not applicable.
[a] Values are presented as percentages or ratio with 95% confidence intervals.

Discussion

- Nephropathy→ multifactorial.
- Contrast media alone(X)
- Intravenous →lesser risk
- In the elderly →decline in renal function + more comorbidities.
- Diabetes was not an independent risk factor in this study.
- Low mean BP was not an independent risk factor in this study

Discussion

- preexisting renal impairment is an independent risk factor for CIN
- CIN is associated with a prolonged hospital length of stay and an increase in hospital and long-term mortality
- At the risk of CIN→ reducing the volume of contrast media, providing preventive measures such as N-acetyl cysteine

Discussion

- Risk greater than 15% would be adequate for any decision making

Limitations

- Patients
- Without external validation
- risk of nephropathy in patients with normal renal function is low (only 2.6%) and most study patients (86.3%) had normal renal function.