Clinical prediction rule for bacteremia among maintenance hemodialysis patients in outpatient settings

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on behalf of "Japanese InvestigatOrs of Innovative Network about Kidney Disease (JOINT-KD)"

Background

- In general population, clinical prediction rules to identify bacteremia were established.
- However, these clinical prediction rules are difficult to use in hemodialysis (HD) patients, since they includes items related to renal function and electrolyte concentration which are affected of the timing of the dialysis. (Eliakim. 2015, Ratzinger. 2014, van Werkhoven. 2014, Takeshima. 2016)
- Further, etiology and pathogen of bacteremia in maintenance HD patients are different from the general population. (Khayr.2003, Nielsen. 2014, Chan.2012, Girndt.2015, Vandecasteele.2009)

Objectives

We aimed to establish a clinical prediction rule (CPR) for bacteremia among HD patients in outpatients settings.

Methods

Study Design: A multi-centre retrospective cohort study

Setting: "Japanese investigators with innovative network about Kidney Disease (JOINT-KD)
six tertiary care institutions and one secondary care institution 【August 2011 ～ July 2013】

Participants: Inclusion criteria

① HD patients who had any set of blood cultures drawn for suspected infection within 24 hr from first arrival at Hp.
② age>=18

Exclusion criteria

① low frequency of hemodialysis (<1 time per week), ② combination of peritoneal dialysis,
③ less than two weeks from the introduction of HD, ④ hospitalized patients referred from another hospital

Outcome: Bacteremia "Identification of bacteria in blood culture specimen w/o fulfilling the definition of bacterial contamination"

Candidate predictors: All candidate predictors were selected thorough literature review

Statistical analysis:

Derivation set "complete dataset for candidate predictors"

- Description
- Conversion of predictors to binary variables
- Development of CPR :

①Select predictors for bacteremia

CPR1; from predictors among **general population** using **step-wise regression** (select items with P<0.05)
CPR2; from predictors among **general population** & **HD patients** using **stepwise regression**
CPR3; from predictors among **general population** & **HD patients** with **clinical expertise**

②Multivariate logistic regression analysis
③Scoring (β-coefficient based)

- Calibration : Hosmer Lemeshow test
- Assessment of test performance

Validation set "bootstrap method (200 interaction)"

- Internal validation : bootstrap method (200 interaction)

Discrimination - C-statistics (95%CI)

Discussion

■ A simple clinical prediction rule specific for HD patients will be helpful for decision making about admission and early ABx administration.

■ Since, "Fistula First" recent awareness campaign for initiation of AVF as vascular access(VA) in HD induction has been promoted by National Kidney Foundation, in the future, it is expected that AVF becomes mainstream in the world.

⇒Our prediction rule developed in Japanese HD cohort, most of VA are AVF, could be a suitable model for the future hemodialysis patients in the world.

■ Bacteremia in HD patients, because they have more simple etiology compared as the general population, were considered to be predictable by simple CPR comprised of small items.

■CPR1 is considered to be clinically easy to use even with excellent predictive ability.

Limitations

- The reasons to draw blood cultures will be undetected.
- Cases with undetectable bacteremia (blood culture negative) could exist.
- Participants will be restricted to tertiary centers.
- Because of the complete dataset analysis, subjects with relatively mild clinical presentation w/o detailed history taking or laboratory test could had been excluded
- Because it is retrospective cohort study, there is uncertainty of the data extracted from the medical records.
- Relatively small number of samples were enrolled.
- External validation was not performed because of small sample size.

Conclusion

We established simple clinical prediction rule for bacteremia among maintenance hemodialysis patients in outpatients settings

Results

Figure 1. Study flow

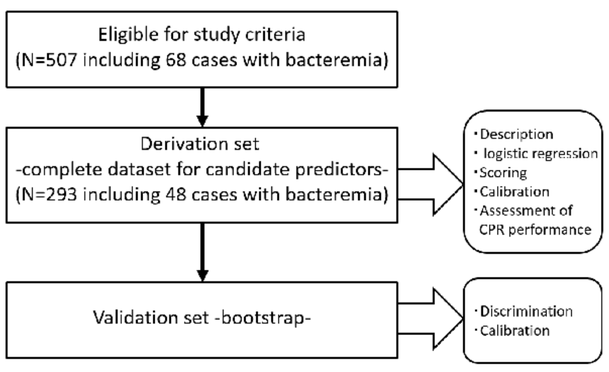

Table 1. Baseline characteristics

	median (quartile or %)		median (quartile or %)
Sex		**Medications**	
Male	195 (66.6)	Steroid use	33 (11.3)
Female	98 (33.5)	Immunosuppressant use	5 (1.7)
Age*	74 (66, 81)	Antibiotics use within 1w*	48 (16.4)
Vital signs		**Symptoms**	
Body temperature*	37.2 (36.6, 38.1)	Chill*	13 (4.4)
Systolic blood pressure*	136 (114, 160)	Nausea*	28 (9.6)
Pulse rate*	84 (74, 100)	Focal abdominal sign*	29 (9.9)
SpO2*	97 (95, 98)	**Causes of CKD**	
(FiO2)	0.21 (0.21, 0.21)	Diabetic nephropathy	123 (42.0)
GCS<15*	45 (15.4)	Hypertensive nephrosclerosis	61 (20.8)
Vintage of HD (month)	61 (23,112)	Chronic glomerulonephritis	45 (15.4)
Vascular access**		Others and unknown	64 (21.8)
AV fistula	245 (83.6)	**Laboratory findings**	
AV graft	28 (9.6)	White blood cell (/μL)*	8400 (5900, 11300)
Superficial artery	16 (5.5)	Platelet count (/μL)*	14.9 (10.5, 20)
Permanent Catheter	4 (1.4)	Albumine (mg/dL)*	3.3 (2.9, 3.6)
Past history of bacteremia**	31 (10.6)	ALP (IU/L)	271 (212, 382)
Comorbidities		Urea nitrogen (mg/dL)	39 (26, 56)
Diabetes mellitus**	131(44.7)	Sodium (mEq/L)*	137 (135, 139)
Malignancy	33 (11.3)	C-reacted protein (mg/dl)*	6.1 (1.8, 12.8)
		Bacteremia	48 (16.3)

* Candidate predictors for bacteremia among general population
** Candidate predictors for bacteremia, specific for HD patients

Table 2. Pathogens of bacteremia

Bacteria	N	Bacteria	N
Staphylococcus aureus	19	***Enterococcus faecalis***	1
Methicillin-sensitive *Staphylococcus aureus*	12	***Pseudomonas aeruginosa***	1
Methicillin-resistant *Staphylococcus aureus*	7	***Streptococcus salivarius***	1
Klebsiella pneumoniae	9	***Streptococcus pneumoniae***	1
Escherichia coli	7	***Streptococcus mutans***	1
Coagulase-negative staphylococcus species	5	***Parabacteroides distasonis***	1
Clostridium perfringens	2	***Helicobacter cinaedi***	1
Bacteroides	2	***Anaerobic gram-negative bacilli***	1
Enterococcus faecium	2		

Table 3. Scoring and calibration

CPR	Selected variables	B-coefficient	95% CI	p-value	Score	Hosmer-Lemeshow χ2test
CPR1	Body temperature ≧ 38.3 ℃	1.12	0.34, 1.91	<0.01	1	
	Pulse rate ≧ 125 /min	1.12	0.01, 2.22	0.04	1	
	CRP ≧10 mg/dL	1.31	0.60, 2.01	<0.01	1	
	ALP > 360 IU/L	1.05	0.35, 1.74	<0.01	1	
	no prior Abx within 1w	1.30	0.15, 2.45	0.03	1	P=0.57
CPR2	Body temperature ≧ 38.3 ℃	1.40	0.63, 2.17	<0.01	1	
	CRP ≧10 mg/dL	1.35	0.64, 2.06	<0.01	1	
	ALP > 360 IU/L	1.08	0.38, 1.78	<0.01	1	
	No prior Abx within 1w	1.44	0.27, 2.61	<0.01	1	
	Past history of bacteremia	1.22	0.29, 2.14	0.01	1	P=0.11
CPR3	Body temperature ≧ 38.3 ℃	0.99	0.22, 1.75	0.01	1	
	Pulse rate ≧125 /min	1.17	0.08, 1.93	0.04	1	
	CRP ≧10 mg/dL	1.35	0.67, 2.0	<0.01	1	
	No prior Abx within 1w	1.23	0.13, 2.44	0.03	1	P=0.4

CPR1: age≧65, GCS≦14, BT ≧38.3, SBP<90, PR≧125, SpO2<90,Focal abdominal sign, chill, nausea, WBC≧15000, Plt<15 × 10^4,ALP>360, Na<130, Alb<3.0, CRP≧10, no prior antibiotics within 1w were entered into a stepwise logistic regression models.
CPR2: age≧65, GCS≦14, BT ≧38.3, SBP<90, PR≧125, SpO2<90, Focal abdominal sign, chill, nausea, WBC≧15000, Plt<15 × 10^4, ALP>360, Na<130, Alb<3.0, CRP≧10, no prior antibiotics within 1w, AVF, past history of bacteremia, DM were entered into a stepwise logistic regression models.
CPR3: age≧65, BT ≧38.3, SBP<90, PR≧125, SpO2<90,chill, nausea, WBC≧15000, CRP≧10, AVF, DM were entered into logistic regression models.

Table 4. Assessment of test performance

CPR	Cutoff	Total	Bacteremia	Sensitivity (95%CI)	Specificity (95%CI)	LR+ (95%CI)	LR- (95%CI)	PPV (95%CI)	NPV (95%CI)
CPR1	≧1	278	48	100 (92.6, 100)	6.1 (3.5, 9.9)	1.1 (1, 1.1)	0	17.3 (13, 22.2)	100 (78.2, 100)
	≧2	162	43	89.6 (77.3, 96.5)	51.4 (45, 57.8)	1.8 (1.6, 2.2)	0.2 (0.1, 0.5)	26.5 (19.9, 34)	96.2 (91.3, 98.7)
	≧3	54	22	45.8 (31.4, 60.8)	86.9 (82.1, 90.9)	3.5 (2.3, 5.5)	0.6 (0.5, 0.8)	40.7 (27.6, 55)	89.1 (84.5, 92.8)
	≧4	9	5	10.4 (3.5, 22.7)	98.4 (95.9, 99.6)	6.4 (1.8, 22.9)	0.9 (0.8, 1)	55.6 (21.2, 86.3)	84.9 (80.2, 88.8)
	≧5	0							
CPR2	≧1	278	48	100 (92.6, 100)	6.1 (3.5, 9.9)	1.1 (1, 1.1)	0	17.3 (13, 22.2)	100 (78.2, 100)
	≧2	173	45	93.8 (82.8, 98.7)	47.8 (41.4, 54.2)	1.8 (1.6, 2.1)	0.1 (0, 0.4)	26 (19.6, 33.2)	97.5 (92.9, 99.5)
	≧3	58	23	47.9 (33.3, 62.8)	85.7 (80.7, 89.8)	3.4 (2.2, 5.1)	0.6 (0.5, 0.8)	39.7 (27, 53.4)	89.4 (84.7, 93)
	≧4	7	4	8.3 (2.3, 20)	98.8 (96.5, 99.7)	6.8 (1.6, 29.4)	0.9 (0.9, 1)	57.1 (18.4, 90.1)	84.6 (79.9, 88.6)
	≧5	0							
CPR3	≧1	271	48	100 (92.6,100)	9.0 (5.7, 13.3)	1.1 (1.1, 1.1)	0	17.7 (13.4, 22.8)	100 (84.6, 100)
	≧2	127	37	77.1 (62.7, 88)	63.3 (56.9, 69.3)	2.1 (1.7, 2.6)	0.4 (0.2, 0.6)	29.1 (21.4, 37.9)	93.4 (88.5, 96.6)
	≧3	21	8	16.7 (7.5, 30.2)	94.7 (91.1, 97.1)	3.1 (1.4, 7.2)	0.9 (0.8, 1)	38.1 (18.1, 61.6)	85.3 (80.5, 89.3)
	≧4	3	3	6.3 (1.3, 17.2)	100 (98.5, 100)	-	0.9 (0.9, 1)	100 (29.2, 100)	84.5 (79.8, 88.5)

Table 5. Results of internal validation

CPR	C-statistics	95%CI
CPR1	0.77	0.70, 0.83
CPR2	0.77	0.68, 0.83
CPR3	0.73	0.64, 0.79

Study facilities

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2. Center for Innovative Research for Communities and Clinical Excellence (CIRC2LE), Fukushima Medical University, Japan.
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4. Division of Nephrology and Hypertension, St. Marianna University, Kawasaki, Japan.

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