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Quantitative evaluation of contrast-induced-nephropathy in vascular post-angiography patients: Feasibility study of a semi-empirical model

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Abstract. In this study, the contrast-induced-nephropathy (CIN) of vascular patients who had undergone angiography was quantitatively evaluated using a semi-empirical model. The model compiled six essential serum readings and biological data from 70 patients in order to develop a 1st-order nonlinear equation with 16 defined terms. The expectation value of the model was used to predict the serum creatinine reading of patients that had been determined to be at high risk of CIN after contrast media (CM) administration. The other five variables included body surface area (BSA), administrated CM, serum creatinine level before CM administration, blood urea nitrogen (BUN), and systolic blood pressure level. A loss function was used to define the difference between the observed and predicted serum creatinine readings after CM administration. The dominant variables were proven to be systolic blood pressure, serum creatinine level before CM administration, and BSA. The cross interaction between the serum creatinine level before CM administration and systolic blood pressure was the decisive term of the model's performance, indicating that both should be specially considered in order to prevent CIN. The BSA, which was usually ignored by medical staff, was also proven to be a significant variable, whereas the BUN reading and amount of injected contrast media were negligible in the semi-empirical model.

Keywords: CIN, BSA, serum creatinine, robust designation, loss function

1. Introduction

In this study, the contrast-induced-nephropathy (CIN) of vascular patients who had undergone angiography was quantitatively evaluated using a semi-empirical model. Radiographic contrast media (CM) are routinely used during numerous procedures, such as computed tomography (CT) scanning,

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angiography, and angioplasty in order to evaluate patients with vascular disease. As a result of these media, some patients develop CIN, an acute decline syndrome that can lead to renal failure. Cardiac angiography, as a diagnostic procedure, is performed under the potential risk of renal failure, especially in patients with preexisting renal insufficiency (RI), diabetes, old age, congestive heart failure, or dehydration. This procedure is risky since high dose of CM must be administrated in order to accurately diagnose patients. Many researchers have studied this phenomenon and attempted to suppress the possibility of CIN by monitoring the blood serum data and medical records of patients. Some researchers have been successfully in preventing CIN. Rashid, et al. [1] administered intravenous N-acetylcysteine in order to suppress the probability of CIN in high-risk patients; this procedure was successful in 44 patients. Kapoor, et al. [2] administered dopamine in renal doses to 40 patients with diabetes in order to prevent the advancement of CIN. In a randomized trial, Vogt, et al. [3] implemented prophylactic hemodialysis after CM administration in order to prevent the advancement of CIN in 113 patients that had been split into two groups. Shyu, et al. [4] evaluated the efficiency of the antioxidant acetylcysteine in limiting nephrotoxicity after coronary procedures based on the medical records of 121 patients. Koc, et al. [5] studied the relationship between serum creatinine level and CIN and attempted to prevent renal failure through a combination of intravenous N-acetylcysteine and varying amounts of hydration.

In this study, a quantified model was established in an attempt to evaluate the serum creatinine readings of vascular patients after undergoing angiography according to six serum levels and biological data. The variables included the body surface area (BSA), administrated CM, serum creatinine level before CM administration, blood urea nitrogen (BUN) level, and systolic blood pressure. The model configuration was established according to a computational program run with SATISTICA [6]. The model compiled the data of seventy male adult vascular patients who had undergone cardiac angiography within the past year and computed a nonlinear 1st-order regression equation fit with sixteen terms in order to obtain a compromised solution. The model was then verified using the data of another group comprised of thirty male adults with similar clinical syndromes.

2. Materials and Methods

2.1. Semi-empirical model

Six essential variable readings were included in this semi-empirical model, defined as (1) A: BSA, (2) B: administrated CM, (3) C: serum creatinine level before CM administration, (4) D: BUN level, (5) E: systolic blood pressure and (6) F: serum creatinine level after CM administration, the expectation value. The mathematical expression was as follows:

$$F = F(A,B,C,D,E,) = a1 \times A + a2 \times B + a3 \times C + a4 \times D + a5 \times E + a6 \times A \times B + a7 \times A \times C + a8 \times A \times D + a9 \times A \times E + a10 \times B \times C + a11 \times B \times D + a12 \times B \times E + a13 \times C \times D + a14 \times C \times E + a15 \times D \times E + a16 \quad (1)$$

As shown in Eq. (1), the configuration of the model was defined in order to correlate the serum creatinine reading after CM administration (F) with the other five variables (A-E) according to either individual variables (a1-a5) or the cross interactions between two variables (a6-a15), resulting in a total of sixteen terms. The serum creatinine level after CM administration is the most important index for CIN prediction. Thus, predicting and suppressing the serum creatinine reading after CM

administration is an important step in preventing CIN. As such, each of the variable readings was needed in order to normalize the variables to the same domain range, within approximately -1 and +1, before computation. This was required during the model configuration in order to unify the dominating contributions of the model.

$$V^* = {V - \frac{V_{max} + V_{min}}{2}} \Big/ {\frac{V_{max} - V_{min}}{2}} \quad (2)$$

In this equation, V^* is the reading of the variable after normalized conversion, and V, V_{max}, and V_{min} are the original reading before conversion, maximum reading, and minimum reading of a specific variable (A-E), respectively. For example, the maximum and minimum readings for BSA were equal to 2.299 and 1.355 m^2, respectively; thus the BSA of case nos. 2 and 9 were converted from their original values, 1.541 and 1.972, to normalized values, -0.557 and 0.326, respectively, according to Eq. (2). The main goal of the normalization process was to create an unified scale ranging from -1.00 to +1.00 so that every specific BSA reading, as well as the readings of the other variables, after normalization would fall within that range.

2.2. Six variables

Table 1 displays the readings of the six essential variables before (original) and after the normalization process (see Eq. (2) for the 70 vascular patients that had undergone angiography in Taichung Armed Forces General Hospital in Taiwan. The BSA ($\sqrt{(H \times W/3600)}$ m^2) was included since human metabolic mechanisms are significantly correlated with BSA. Large BSA and BMI values are interpreted as high fluid and solute turnover rates in humans [7]. The administered CM was an IOPAMIRO 370 injection (Bracco S.P.A. Italy) [8]. Serum creatinine is an important indicator of renal health since it is an easily measured byproduct of muscle metabolism that is excreted unchanged by the kidneys. Creatinine itself is produced via a biological system involving creatine, phosphocreatine (also known as creatine phosphate), and adenosine triphosphate (ATP, the body's immediate energy supply). Creatinine is primarily removed from the blood by the kidneys mostly through glomerular filtration, but also through proximal tubular secretion. Little or no tubular creatinine reabsorption occurs. If filtration by the kidneys is deficient, serum creatinine levels rise [9]. BUN readings are also an indication of renal health. The liver produces urea during the urea cycle as a waste product of protein digestion. Normal human adult blood should contain between 6 and 20 mg/dL of blood. Blood pressure varies depending on situation, activity, and disease states; thus, the blood pressure inside blood vessels during heart beats is always an important index. As shown in Table 1, the readings in every normalized column varied between -1.00 and +1.00 and thereby provided equal contribution to the computational model.

2.3. STATISTICA program

In this study, the semi-empirical model was run with the STATISTICA program [6]. The correlations among the variables (see Eq. (1) were determined and defined as nonlinear models, nonlinear estimations, and user-specified regressions with customized loss functions in order to perform a numerical analysis using the normalized data of the 70 patients. The predicted serum creatinine readings after CM administration were the expectation values of the computational results. Therefore, 350 individual data points [5×70=350] were included in the model in order to optimize the

compromised solution array [70×1=70] of the serum creatinine reading after CM administration. In addition, sixteen items, including one constant, were used in the semi-empirical model in order to indicate any correlation among the variables. The loss function was defined as the total deviation between the observed and predicted serum creatinine readings after CM administration for all 70 cases.

Table 1

The readings of the six essential variables before (original) and after the normalization process (see Eq. (2) for the 70 vascular patients that had undergone angiography in Taichung Armed Forces General Hospital in Taiwan. The last column shows the predicted serum creatinine reading after CM administration

	Original						**Normalized**						**Predicted**
se No	**BSA**	**Contrast media**	**Serum Creatinine before**	**BUN**	**Systolic blood pressure**	**Serum Creatinine after**	**BSA**	**Contrast media**	**Serum Creatinine before**	**BUN**	**Systolic blood pressure**	**Serum Creatinine after**	**Serum Creatinine after**
	[m^2]	[mL]	[mg/dL]	[mg/dL]	[mmHg]	[mg/dL]	[m^2]	[mL]	[mg/dL]	[mg/dL]	[mmHg]	[mg/dL]	[mg/dL]
1	1.619	130	1.15	14.70	124	1.36	-0.396	-0.636	-0.809	-0.814	-0.592	-0.844	1.18
2	1.541	190	4.09	71.30	181	8.31	-0.557	-0.273	0.054	1.000	0.211	0.856	2.03
3	1.601	300	0.55	17.34	138	0.89	-0.433	0.394	-0.985	-0.729	-0.394	-0.958	1.62
4	1.523	200	1.28	22.80	136	1.34	-0.594	-0.212	-0.771	-0.554	-0.423	-0.848	1.05
5	1.699	140	1.58	26.07	125	1.88	-0.231	-0.576	-0.683	-0.449	-0.577	-0.716	1.19
6	1.904	100	0.69	11.40	132	0.82	0.189	-0.818	-0.944	-0.919	-0.479	-0.976	1.19
7	2.279	100	1.20	16.60	165	1.25	0.958	-0.818	-0.794	-0.753	-0.014	-0.870	1.04
8	1.956	170	0.99	12.70	113	1.28	0.296	-0.394	-0.856	-0.878	-0.746	-0.863	1.29
9	1.972	80	0.86	9.20	141	0.85	0.329	-0.939	-0.894	-0.990	-0.352	-0.968	0.99
10	1.749	120	1.10	23.60	135	0.99	-0.129	-0.697	-0.824	-0.528	-0.437	-0.934	0.90
11	1.725	100	7.31	35.20	144	7.35	-0.179	-0.818	1.000	-0.157	-0.310	0.621	1.01
12	2.114	90	0.92	17.70	144	0.94	0.620	-0.879	-0.877	-0.717	-0.310	-0.946	1.02
13	1.665	100	1.41	16.90	132	1.93	-0.301	-0.818	-0.733	-0.743	-0.479	-0.704	1.37
14	1.450	120	1.02	15.40	150	1.05	-0.743	-0.697	-0.847	-0.791	-0.225	-0.919	1.03
15	1.721	200	1.09	16.50	183	1.39	-0.187	-0.212	-0.827	-0.756	0.239	-0.836	1.28
16	1.765	100	1.20	34.00	115	1.22	-0.096	-0.818	-0.794	-0.195	-0.718	-0.878	1.02
17	1.694	150	1.10	21.00	111	1.77	-0.242	-0.515	-0.824	-0.612	-0.775	-0.743	1.61
18	1.915	110	1.14	20.35	155	1.24	0.211	-0.758	-0.812	-0.632	-0.155	-0.873	1.09
19	1.949	380	1.05	13.00	190	1.23	0.282	0.879	-0.838	-0.868	0.338	-0.875	1.17
20	1.573	80	1.32	23.30	124	1.33	-0.490	-0.939	-0.759	-0.538	-0.592	-0.851	1.01
21	1.549	70	1.15	17.80	106	1.08	-0.540	-1.000	-0.809	-0.714	-0.845	-0.912	0.94
22	1.597	90	1.25	26.50	151	1.51	-0.441	-0.879	-0.780	-0.435	-0.211	-0.807	1.21
23	1.772	180	0.88	13.70	141	0.93	-0.081	-0.333	-0.888	-0.846	-0.352	-0.949	1.06
24	1.626	100	1.13	27.40	138	1.38	-0.382	-0.818	-0.815	-0.407	-0.394	-0.839	1.22
25	2.025	190	0.78	15.80	113	1.11	0.437	-0.273	-0.918	-0.778	-0.746	-0.905	1.42
26	1.794	175	1.08	14.90	121	1.15	-0.036	-0.364	-0.830	-0.807	-0.634	-0.895	1.06
27	1.735	160	1.27	17.78	124	1.46	-0.158	-0.455	-0.774	-0.715	-0.592	-0.819	1.15
28	1.763	260	0.72	9.71	180	0.97	-0.101	0.152	-0.935	-0.973	0.197	-0.939	1.35
29	1.926	190	2.75	38.72	160	2.98	0.234	-0.273	-0.339	-0.044	-0.085	-0.447	1.08
30	2.190	230	0.85	18.80	178	0.89	0.776	-0.030	-0.897	-0.682	0.169	-0.958	1.05
31	1.511	320	1.03	18.76	162	1.28	-0.619	0.515	-0.844	-0.683	-0.056	-0.863	1.24
32	1.752	130	0.77	15.40	156	0.80	-0.123	-0.636	-0.921	-0.791	-0.141	-0.980	1.04
33	1.797	180	1.13	17.20	133	1.12	-0.030	-0.333	-0.815	-0.733	-0.465	-0.902	0.99
34	1.325	160	0.75	30.60	101	0.72	-1.000	-0.455	-0.927	-0.304	-0.915	-1.000	0.96
35	2.128	250	0.69	13.72	136	0.94	0.649	0.091	-0.944	-0.845	-0.423	-0.946	1.36
36	1.730	220	1.06	14.20	170	1.26	-0.167	-0.091	-0.836	-0.830	0.056	-0.868	1.19
37	1.616	400	0.97	9.63	148	1.39	-0.403	1.000	-0.862	-0.976	-0.254	-0.836	1.43
38	1.998	170	0.82	12.80	127	0.97	0.381	-0.394	-0.906	-0.874	-0.549	-0.939	1.18
39	1.528	110	2.33	28.30	137	2.30	-0.584	-0.758	-0.463	-0.378	-0.408	-0.614	0.99
40	1.809	170	1.61	18.00	114	1.75	-0.005	-0.394	-0.674	-0.708	-0.732	-0.748	1.09
41	1.873	210	1.24	29.00	158	1.36	0.125	-0.152	-0.783	-0.355	-0.113	-0.844	1.10
42	1.835	180	1.21	18.40	129	1.46	0.047	-0.333	-0.791	-0.695	-0.521	-0.819	1.21
43	2.084	180	0.99	12.83	133	1.26	0.559	-0.333	-0.856	-0.873	-0.465	-0.868	1.27
44	1.873	200	1.02	10.57	150	1.13	0.126	-0.212	-0.847	-0.946	-0.225	-0.900	1.11

45	1.504	180	0.93	23.70	139	1.13	-0.632	-0.333	-0.874	-0.525	-0.380	-0.900	1.22
46	1.851	230	0.99	20.39	150	1.58	0.081	-0.030	-0.856	-0.631	-0.225	-0.790	1.60
47	1.892	150	2.08	29.10	146	2.12	0.163	-0.515	-0.536	-0.352	-0.282	-0.658	1.02
48	1.942	220	1.07	16.00	115	1.62	0.268	-0.091	-0.833	-0.772	-0.718	-0.780	1.51
49	1.865	210	1.40	15.00	160	1.43	0.109	-0.152	-0.736	-0.804	-0.085	-0.826	1.02
50	1.713	200	0.95	12.59	114	0.92	-0.204	-0.212	-0.868	-0.881	-0.732	-0.951	0.97
51	1.852	150	0.88	16.21	148	1.27	0.083	-0.515	-0.888	-0.765	-0.254	-0.866	1.44
52	1.628	240	1.07	28.50	152	1.15	-0.378	0.030	-0.833	-0.371	-0.197	-0.895	1.07
53	1.559	300	0.99	16.00	150	1.30	-0.520	0.394	-0.856	-0.772	-0.225	-0.858	1.31
54	1.974	150	0.90	17.47	105	2.15	0.333	-0.515	-0.883	-0.725	-0.859	-0.650	2.39
55	1.760	350	1.66	15.30	163	2.11	-0.106	0.697	-0.659	-0.794	-0.042	-0.660	1.27
56	1.673	180	0.93	12.53	130	1.26	-0.285	-0.333	-0.874	-0.883	-0.507	-0.868	1.35
57	1.815	180	0.83	17.20	132	0.89	0.006	-0.333	-0.903	-0.733	-0.479	-0.958	1.07
58	1.752	120	3.04	42.46	237	7.88	-0.122	-0.697	-0.254	0.076	1.000	0.751	2.59
59	1.426	170	2.18	36.50	110	1.92	-0.793	-0.394	-0.507	-0.115	-0.789	-0.707	0.88
60	1.843	230	1.06	10.07	137	0.77	0.063	-0.030	-0.836	-0.962	-0.408	-0.988	0.73
61	1.586	200	1.47	16.30	112	1.47	-0.463	-0.212	-0.715	-0.762	-0.761	-0.817	1.00
62	2.127	200	0.96	15.21	159	0.80	0.646	-0.212	-0.865	-0.797	-0.099	-0.980	0.83
63	1.903	180	1.25	12.54	148	1.24	0.187	-0.333	-0.780	-0.883	-0.254	-0.873	0.99
64	1.700	180	0.99	22.80	113	1.22	-0.229	-0.333	-0.856	-0.554	-0.746	-0.878	1.23
65	1.793	150	0.89	8.88	155	0.75	-0.039	-0.515	-0.885	-1.000	-0.155	-0.993	0.84
66	1.944	280	0.98	19.90	95	0.89	0.270	0.273	-0.859	-0.647	-1.000	-0.958	0.91
67	2.299	360	0.89	14.82	138	0.94	1.000	0.758	-0.885	-0.810	-0.394	-0.946	1.06
68	1.912	140	0.91	15.18	144	0.83	0.206	-0.576	-0.880	-0.798	-0.310	-0.973	0.91
69	1.745	170	1.04	16.67	184	0.91	-0.139	-0.394	-0.841	-0.750	0.254	-0.954	0.88
70	1.944	180	1.61	27.50	195	1.27	0.270	-0.333	-0.674	-0.403	0.408	-0.866	0.79

3. Results

The last column of the Table 1 shows the predicted serum creatinine reading after CM administration. The data was calculated using the regressed semi-empirical model (see Eq. (1). The predicted data corresponded well with the original data (Table 1, column 7) indicating that the model did not result in any systematic mistake in the primary definition or any runtime errors during the analyzing process. Table 2 lists the regressed coefficients of all sixteen terms. As shown in Table 2, the ranks of the normalized coefficients were also listed for reference. Dominant variables were defined to be variables with large coefficients in the regression analysis; thus, the most dominant variables included the systolic blood pressure (E, ranked 2), serum creatinine before CM administration (C, ranked 3), and BSA (A, ranked 4); in contrast, the CM administered (B, ranked 11) and BUN (D, ranked 12) only slightly affected the resulting model. The cross interactions among the variables also strongly affected the model's performance. The serum creatinine reading before CM administration and systolic blood pressure cross interaction (C×E, ranked 1) were most strongly correlated, whereas the BSA and Serum Creatinine before administration (A×C, ranked 5), CM and systolic blood pressure (B×E, ranked 6), and BSA and systolic blood pressure (A×E, ranked 7) cross interactions were moderately correlated and also measurable affected the model's performance.

The model yielded another regression result that included all of the coefficients when that data normalization process was bypassed (see Table 1 and Eq. (2)), as shown in Table 2 (column 4 and 5 under the original subtitle). However, without the normalization process, correlation did not exist among the coefficients. Ranking orders cannot imply the actual contributions of variables. Moreover, eight of the sixteen coefficients were approximately zero, implying that the contributions of the corresponding variables were either irrelevant or negligible. The computed results would have to be carefully interpreted in order to prevent misunderstanding.

Table 2

The regressed coefficients of all sixteen terms. The ranks of the normalized coefficients were also listed for reference

Parameter	variable	Coefficient	Original		Normalized	
			value	Rank	value	Rank
BSA	A	a1	4.369	1	-0.547	4
Contrast media	B	a2	0.001		-0.085	11
Serum Creatinine (before)	C	a3	0.176	4	1.070	3
BUN	D	a4	-0.023	5	0.059	12
Systolic blood pressure	E	a5	-0.011		1.206	2
BSA × Contrast media	A×B	a6	-0.003		-0.066	8
BSA × Serum Creatinine (before)	A×C	a7	-1.361	3	-0.552	5
BSA × BUN	A×D	a8	-0.001		-0.004	15
BSA × Systolic blood pressure	A×E	a9	-0.017	7	-0.144	7
Contrast media × Serum Creatinine (before)	B×C	a10	0.000		-0.046	13
Contrast media × BUN	B×D	a11	0.000		-0.133	9
Contrast media × Systolic blood pressure	B×E	a12	0.000		0.142	6
Serum Creatinine (before) × BUN	C×D	a13	0.000		0.001	16
Serum Creatinine (before) × Systolic blood	C×E	a14	0.022	6	1.301	1
BUN × Systolic blood pressure	D×E	a15	0.000		0.186	10
constant		a16	-2.115	2	0.045	14

4. Discussion

4.1. Model verification

Data was obtained from an additional group comprised of 30 male adult vascular patients in order to verify the derived model. The BSA, systolic blood pressure, and age p-test results indicated that no significant differences existed between the two groups. The BSA, systolic blood pressure, and age p-test were equal to 0.84, 0.73, and 0.32, respectively. Table 3 displays the data used for verification. As shown in Table 3, some of the readings after normalization exceeded 1.00, including that of case no. 24 (serum creatinine level before CM administration) and case nos. 4, 14, and 24 (serum creatinine after CM administration). This was because the acquired data was outside the minimum and maximum readings of those specific variables in the original group (see Table 1). The predicted serum creatinine reading after CM administration and its relative discrepancy (%) from the observed serum creatinine reading after CM administration are listed in the last two columns of Table 3. Only one of the thirty predicted datasets exhibited relative discrepancies greater than 100%. Most of the relative discrepancies (23 out of 30) were less than 30%. Figure 1 illustrates the correspondence between the observed and predicted serum creatinine reading after CM administration for original and verification groups. The regression lines of the observed and predicted serum creatinine readings depicted a high degree of linearity, which is specified by the derived coefficient of determination (r^2). A perfect straight line has an r^2 value of 1.00. The coefficients of determination (r^2) were high ($r^2 = 0.968$) in this study.

4.2. Robust designation in model configuration

The semi-empirical model proposed in this study was constructed according to robust designation. The normalization of the serum levels and biological data improved the robustness of the system and simulated the loss function in reality [10]. Loss functions are used to identify any deviations between experimental and desired values. By unifying the domains of the involved variables, their specific contributions were accurately depicted; thus, from a robust designation viewpoint, the derived

Table 3

The 30 male adult vascular patients for verification. Some of the readings after normalization exceeded 1.00. The predicted serum creatinine reading after CM administration and its relative discrepancy (%) from the observed serum creatinine reading after CM administration are listed in the last two columns.

	Original						Normalized						Predicted	
Case No	BSA	Contrast media	Serum Creatinine before	BUN	Systolic blood pressure	Serum Creatinine after [A]	BSA	Contrast media	Serum Creatinine before	BUN	Systolic blood pressure	Serum Creatinine after	Serum Creatinine after [B]	[(A-B)/A] 100%
	[m^2]	[mL]	[mg/dL]	[mg/dL]	[mmHg]	[mg/dL]	[m^2]	[mL]	[mg/dL]	[mg/dL]	[mmHg]	[mg/dL]	[mg/dL]	
1	1.654	300	1.37	25.50	140	4.09	-0.324	0.394	-0.757	-0.467	-0.366	-0.112	3.54	13.38
2	2.068	140	0.92	17.20	124	0.87	0.525	-0.576	-0.891	-0.733	-0.592	-0.960	0.87	-0.33
3	1.759	130	0.84	26.90	117	0.96	-0.109	-0.636	-0.914	-0.423	-0.690	-0.937	2.01	-108.97
4	1.911	75	0.61	16.00	118	0.64	0.204	-0.970	-0.982	-0.772	-0.676	-1.021	0.56	11.96
5	2.138	250	1.19	14.90	190	1.57	0.670	0.091	-0.811	-0.807	0.338	-0.776	1.18	25.14
6	1.764	80	1.28	29.70	115	1.37	-0.099	-0.939	-0.784	-0.333	-0.718	-0.829	1.26	7.75
7	1.854	130	1.06	23.00	127	1.03	0.086	-0.636	-0.849	-0.548	-0.549	-0.918	0.94	8.91
8	1.729	80	1.12	25.80	131	1.01	-0.171	-0.939	-0.831	-0.458	-0.493	-0.924	0.25	75.24
9	1.775	130	0.83	13.12	153	0.95	-0.076	-0.636	-0.917	-0.864	-0.183	-0.939	0.71	25.45
10	1.534	180	1.21	24.80	144	1.43	-0.571	-0.333	-0.805	-0.490	-0.310	-0.813	2.39	-67.24
11	1.992	200	0.73	9.21	129	0.87	0.369	-0.212	-0.947	-0.989	-0.521	-0.960	0.62	29.22
12	1.838	90	0.78	16.65	123	0.94	0.054	-0.879	-0.932	-0.751	-0.606	-0.942	0.69	27.11
13	1.742	145	1.00	18.00	142	1.04	-0.144	-0.545	-0.867	-0.708	-0.338	-0.916	0.92	11.13
14	1.986	150	0.90	13.28	140	0.69	0.357	-0.515	-0.896	-0.859	-0.366	-1.008	0.77	-12.08
15	1.726	150	0.94	19.80	133	0.89	-0.176	-0.515	-0.885	-0.650	-0.465	-0.955	1.17	-30.98
16	1.812	100	0.93	24.70	119	0.85	0.001	-0.818	-0.888	-0.493	-0.662	-0.966	0.94	-10.42
17	1.802	130	0.99	15.50	138	1.10	-0.020	-0.636	-0.870	-0.788	-0.394	-0.900	0.89	19.04
18	1.504	120	0.96	17.60	174	1.18	-0.633	-0.697	-0.879	-0.721	0.113	-0.879	1.24	-4.74
19	1.504	120	0.96	17.60	162	1.92	-0.633	-0.697	-0.879	-0.721	-0.056	-0.684	1.17	39.04
20	1.726	100	1.53	28.30	125	1.38	-0.176	-0.818	-0.710	-0.378	-0.577	-0.826	1.27	8.23
21	1.873	100	1.18	31.03	120	1.37	0.125	-0.818	-0.814	-0.290	-0.648	-0.829	0.92	32.99
22	1.660	130	0.88	13.91	167	0.98	-0.312	-0.636	-0.902	-0.839	0.014	-0.931	1.05	-7.21
23	2.020	220	1.04	17.14	108	1.00	0.428	-0.091	-0.855	-0.735	-0.817	-0.926	1.11	-11.08
24	1.621	200	0.50	32.33	111	8.90	-0.393	-0.212	-1.015	-0.249	-0.775	1.155	8.27	7.1
25	1.647	180	1.07	15.50	135	0.94	-0.340	-0.333	-0.846	-0.788	-0.437	-0.942	1.05	-11.49
26	1.992	130	1.40	23.00	155	1.18	0.369	-0.636	-0.749	-0.548	-0.155	-0.879	1.07	9.15
27	1.938	120	2.49	36.55	103	3.87	0.258	-0.697	-0.426	-0.113	-0.887	-0.170	3.69	4.56
28	1.764	210	0.96	15.76	170	1.87	-0.099	-0.152	-0.879	-0.780	0.056	-0.697	1.53	18.09
29	1.595	100	1.36	33.24	133	1.34	-0.445	-0.818	-0.760	-0.219	-0.465	-0.837	1.17	12.55
30	1.880	100	1.07	21.81	130	1.06	0.140	-0.818	-0.846	-0.586	-0.507	-0.910	0.56	47.22

coefficients represented the dominance of the specific variables in reality and reduced the loss function of the model. In contrast, the last constant in the model (see Eq. (1) could be interpreted as the partial contribution of those undefined remainders since the correlation could have been too complicated to define or too fluctuated to quantify. The derived constant of the model was equal to 0.045 (ranked 14), indicating not only that the contribution from this item could be ignored since it barely affected the performance of the model, but also that the variables ranked lower than 14, such as BSA×BUN (ranked 15) or serum creatinine (before)×BUN (ranked 16), contributed to the model even less. This model could be further developed by expanding the contributions from the dominant variables while still providing reasonable prediction so that a comparatively small constant term would imply a low systematic error.

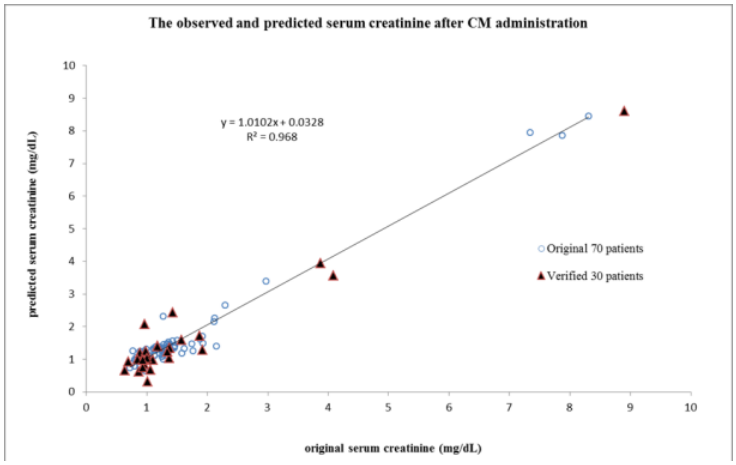

Fig. 1. The correspondence between the observed and predicted serum creatinine reading after CM administration for original and verification groups. The regression lines of the observed and predicted serum creatinine readings depicted a high degree of linearity.

4.3. Dominant variables

4.3.1. Systolic blood pressure

The pressure of blood circulating to the kidneys increases when the blood pressure increases. The kidneys cannot tolerate high blood pressure level since they are delicately structure organs. Furthermore, the kidneys filter large volumes of blood and, therefore, are very sensitive to changes in blood pressure. The kidneys can suffer from hypoxia or even become necrosis when the blood pressure is continuously low. In contrast, when the blood pressure is too high, the kidneys are damaged and proteinuria level can increase, resulting in renal tubule constriction, sclerosis and renal damage. This type of damage accumulates over time; thus, as a first step, high blood pressure should be controlled in order to reduce pressure exerted on the kidneys.

In one study, Dr. Perry analyzed 11,912 cases of early-stage hypertension ranging from 1974 to 1976 and discovered that the long term management of systolic blood pressure can effectively affect the later stages of Nephropathy [11]. From a physiological viewpoint, hypertension can cause afferent arterioles to systole. The systole of afferent arterioles can result in glomerular, renal tubule and avascular necrosis. This furthermore develops into loss function of kidney function and the development of renal atrophy and fibrosis. Thus, systolic blood pressure is the most important factor contributing to renal function

4.3.2. Serum creatinine

Serum creatinine reading is a highly stable measurement and indicator of renal function that is commonly used to evaluate the seriousness of renal dysfunction and monitor the progression of kidney diseases. Patients with continuously high serum creatinine readings often have an irreversible loss of kidney function. Serum creatinine is primarily derived from muscular activity and metabolism. The serum creatinine created by the body is filtered daily by the kidneys and excreted through urine. Therefore, if the kidneys are unable to entirely filter and excrete the normal daily amount of creatinine created by the body, the serum creatinine level increases. Serum creatinine readings are related to muscle mass. In addition, serum creatinine readings are a more accurate measurement than BUN

readings in determining kidney function. According to the definition of glomerular filtration rate (GFR) [(0.55×Height (cm))/(Scr (mg/dl))] given by Schwartz, as the serum creatinine level of a patient increases, the GFR decreases. If a patient's GFR is continuously less than 60 ml/ min /1.73 m^2 for three months or longer, the patient is clinically diagnosed with chronic renal disease. Therefore, serum creatinine is a very important measurement and indicator of the existence of kidney disease [12-14].

4.3.3. BSA

The BSA values provided a negligible amount of information regarding the routinely vascular patients that had undergone cardiac angiography. However, from a physiology viewpoint, serum **c**reatinine is a byproduct of the metabolic mechanism of muscular activity, and large BSA values imply large amount of muscular tissue. Therefore, BSA values should still be considered during CM administration in order to prevent CIN. Furthermore, according to the derived model, BSA was ranked fourth in variable dominance (see Table 2).

5. Conclusion

In this study, the CIN of vascular patients that had undergone angiography was quantitatively calculated using a semi-empirical model. The model was defined by 16 terms, comprised of 6 individual variables and their cross interactions. The coefficients of the semi-empirical model were derived from a regression analysis performed with STATISTICA using the data of 70 male adult vascular patients that had undergone angiography within the last year. The model's performance was verified using the data of another group of 30 patients with similar clinical syndromes. The loss function of the model was defined as the deviation between the observed and predicted serum creatinine readings after CM administration. The dominant variables included the systolic blood pressure, serum creatinine reading before CM administration, and BSA. The BUN reading and amount of injected CM did not significantly affect the model's performance.

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