Convolution Neural Network for Renal Function Assessment Based on Glomerular Filtration Rate

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Abstract. Objective: To develop a Convolution Neural Network (CNN) and discuss its performance in the estimation of Glomerular Filtration Rate (GFR) for patients with chronic kidney disease (CKD).

Methods: A total of 112 patients with chronic kidney disease were enrolled in this study. The GFR is measured by 99mTc-DTPA renal dynamic and used as standard GFR after normalization by body surface area imaging. We established a CNN model and verified the performance of the model by comparing the GFR predicted by the model with the standard GFR. It turned out that the CNN could better evaluate the GFR of patients which is superior to the CG formula, MDRD formula, CKD-EPI formula and GRNN model.

Conclusions: The CNN significantly evaluated GFR for patients with CKD, and it showed better performance than traditional methods and GRNN model and closer to the results of 99mTc-DTPA. The experimental results demonstrated that CNN could be used to estimate GFR.

1. Introduction
Chronic kidney disease (CKD) is a public health problem that deserves widespread attention worldwide. The prevalence of CKD is high, and the treatment cost in the later stage of CKD is a heavy economic burden. In addition, the early symptoms of CKD are not obvious and there are no special manifestations, which leads to the low early awareness rate, diagnosis rate and treatment rate of CKD. Once diagnosed, it is moderate and severe CKD, which seriously affects the early diagnosis and treatment of CKD. At present, there is no strong and effective treatment for CKD. So early detection, early diagnosis, early intervention and delaying the process are particularly important.

GFR is not only the best index to reflect renal function, but also the main basis to judge the stage of renal function. Accurate evaluation of GFR is of great significance in clinical practice and research. Inulin clearance is the gold standard for GFR determination. The clearance rate of isotopic markers is the main standard for the determination of GFR. However, the expensive price of inulin and the radioactivity of isotope labeling limit their use in GFR detection. Now, renal dynamic imaging is commonly used to evaluate GFR. However, this method requires the injection of radioisotope markers and consumes a lot of water to promote the excretion of markers. Furthermore it is not suitable for pregnant women and limits its
clinical application. Many traditional linear regression equations, such as formula [1] Cock-croft-Gault (CG), formula [2] MDRD, formula [3] CKD-EPI, formula [4] filler, formula [5] Hoek, etc. are calculated based on demographic variables (age, gender, race), fluorescent markers (serum creatinine (Scr) and cystatin C). However, the GFR calculated by these formulas lacks consistent accuracy.

With the rapid development of artificial intelligence technology, the combination of medicine and industry is an inevitable trend in the future. Y W Chen et al. [6] first applied the neural network model to GFR estimation. This study proved that BP neural network can fit the simplified equation of MDRD, and proved the strong approximation ability of BP neural network and the feasibility of applying BP neural network to GFR estimation.

Neural network has made many research achievements in estimating GFR. WASD neural network model [7] and improved RBF excited WASD neural network model [8] proposed by Y N Zhang et al. H Y Zou et al. proposed an adaptive fuzzy neural network model for feature selection [9]. Artificial neural network model [10] proposed by N S Li et al. Improved artificial neural network [11] proposed by X Liu et al. Radial basis function (RBF) neural network model [12-13] proposed by X Liu et al., J Xu et al. However, with the deepening of research, the disadvantages of these methods are gradually revealed. Among them, BP neural network is prone to local optimal solution and 'over fitting' problem. In most cases, RBF neural network is difficult to map the real input-output relationship, and the optimization process may be ill conditioned. The generalized regression neural network is a variation of RBF neural network, and the same problem may occur. In recent years, because the convolution neural network (CNN) is a deep feedforward neural network with the characteristics of local connection and weight sharing, it is widely used in the fields of computer vision, natural language processing, speech recognition and so on. Therefore, CNN was applied to estimate GFR and compared with the traditional methods CG equation, MDRD equation, CKD-EPI equation and GRNN model. This paper aims to explore an efficient and accurate GFR estimation method.

2. Data and Methods:

2.1. Clinical Data
A total of 112 patients were treated in the Second Hospital of Anhui Medical University from May 2019 to December 2020. Among them, there are 69 males, accounting for 61.6% of the total number, and 43 females, accounting for 38.4% of the total number. Based on literature reports and clinical experience, gender, age (year), height (CM), weight (kg) and uric acid(μmol/L), serum creatinine (Scr, μmol/L), urea nitrogen(BUN, mmol/L), Cystatin C (CysC, mg/L) and globulin(GLB, g/L) related to the change of glomerular filtration rate were selected as the characteristics of this study, and the GFR measured by body surface area standardized renal dynamic imaging was used as the standard mGFR (ml / (min∙1.73m^2)). According to the correlation between each variable and mGFR (Table 1). The characteristics with good correlation such as age, Scr, BUN and CysC are finally selected as the input characteristics of the network.

| Features         | Gender | Age  | Height | Weight | Uric acid | Scr   | BUN  | CysC | GLB |
|------------------|--------|------|--------|--------|-----------|-------|------|------|-----|
| Relevance        | 0.240  | -0.429 | -0.058 | -0.059 | -0.347    | -0.557 | -0.403 | -0.394 | 0.014 |

* express p < 0.05, the correlation is significant.
** express p < 0.01, the correlation is significant.

2.2. Statistical Methods
All data were analyzed using medcalc and SPSS 24.0. Among them, K-S test was used to test the normal
distribution of variables. If it obeys the normal distribution, T-test of paired design was adopted, and the variables were expressed in $x \pm s$. If it obeys skew distribution, Wilcoxon rank sum test was adopted, and the variables were expressed in $(Q_1, Q_3)$. Pearson correlation analysis was used to analyze the correlation between variables and mGFR. The 95% consistency of the eGFR and mGFR of each formulation was based on the Bland Altman drawing method, and the acceptable professional value of the consistency limit was set to twice the CKD stage limit [60mL/(min·1.73m²)]. The evaluation of eGFR value took deviation (average of each formula minus mGFR) and accuracy (15%, 30%, 50% coincidence rate) that was the percentage of cases where the estimated GFR of each formula falls within the range of ±15%, ±30%, ±50% of mGFR. Compared the accuracy of eGFR and mGFR using F-test. Z-test was used to compare the coincidence rate. P<0.05 and P<0.01 indicated that the difference is statistically significant.

2.3. Calculation of Each GFR Evaluation Equation
The purpose of this study was to verify the applicability and superiority of CNN model in estimating GFR. Through the literature report [14-16], selected Cock-croft-Gault (CG) formula, MDRD formula and CKD-EPI formula which are commonly used in Chinese GFR estimation to compare with the GFR predicted by the CNN model. See Table 2 for each equation formula.

2.4. CNN Model
The experimental data set contains 112 case data. According to the principle of random selection, it is divided into training set and test set according to the ratio of 7:3. There are 78 case data in the training set and 34 case data in the test set. Using keras environment and python language to build CNN model as a tool to study and estimate GFR model. Age, Scr, BUN and CysC are four variables as inputs, and the model has only one output variable eGFR. The statistics of each variable are shown in Table 3.

Table 2. Three eGFR formulas.

| Formula     | Gender | Scr/μmol/L | Formula                                                                 |
|-------------|--------|------------|--------------------------------------------------------------------------|
| CKD-EPI     | female | ≤0.7       | $144 \times (Scr/0.7)^{0.125} \times 0.993^{female}$                    |
|             | female | >0.7       | $144 \times (Scr/0.7)^{1.206} \times 0.993^{female}$                    |
|             | male   | ≤0.9       | $141 \times (Scr/0.7)^{0.411} \times 0.993^{male}$                      |
|             | male   | >0.9       | $144 \times (Scr/0.7)^{1.206} \times 0.993^{male}$                      |
| MDRD        |        |            | $eGFR_{MDRD} = 175 \times Scr^{-1.154} \times age^{-0.203} \times (0.742f) \times (1.212b)$ |
| C-G         |        |            | $[(140 -age)\times weight]/(Scr \times 72)(female \times 0.85)$           |

Table 3. Basic information of GFR dataset ($\bar{x} \pm s$).

| Sample     | Numbers | age/year | Scr/μmol/L | BUN/mmol/L | CysC/mg/L | mGFRmL/(min·1.73m²) |
|------------|---------|----------|------------|------------|-----------|---------------------|
| Train set  | 78      | 51.31    | 88.28      | 5.98 ± 1.95| 0.94      | 86.47 ± 42.64       |
|            | ± 13.88 |          | ± 31.66    |            | ± 0.44    |                     |
| Test set   | 34      | 54.56    | 91.94      | 6.44 ± 2.41| 1.04      | 78.91 ± 40.02       |
|            | ± 12.85 |          | ± 38.08    |            | ± 0.49    |                     |
| Population | 112     | 52.29    | 89.39      | 6.12 ± 2.10| 0.97      | 84.18 ± 41.82       |
|            | ± 13.60 |          | ± 33.60    |            | ± 0.45    |                     |
Convolutional Neural Network is a kind of neural network with supervised learning. Its basic structure is composed of five parts: input layer, convolution layer, pooling layer, full connection layer and output layer. Among them, convolution layer is the most important layer in neural network, which is used to extract features. At the same time, the characteristic of incomplete connection and parameter sharing of convolution layer greatly reduces the network parameters, ensures the sparsity of the network and prevents over-fitting. After convolution output, bias is usually added and nonlinear activation function is introduced. After the activation function, the output result is:

\[ Z_{x,y} = \delta \left( \sum_{i} m_i \cdot n_i + b \right) \]  

(1)

Where equation (1) was the output eigenvalue of point \((x, y)\) in the spatial coordinate of layer \(J\). The size of convolution kernel is \(p \times q\), the value of convolution kernel is \(m_i\), and the size of weight is the characteristic offset, \(\delta()\) is the activation function. Because the input and output of the estimation GFR problem are numerical signals and the convolution kernel are one-dimensional convolution kernel.

The main function of pooling layer is to down sample the features extracted by convolution layer, which can remove redundant information and compress the features; And it can expand the receptive field and realize invariance. At present, there are mainly two methods: maximum pooling and average pooling. The maximum pool method was used in this experiment.

Model Establishment. The parameter settings of the whole model are shown in Table 4. In order to avoid the gradient disappearing and neuron saturation in the process of feature learning, all activation functions are set as relu functions. The whole process goes through four feature extraction processes, and each feature extraction includes two convolution layers and a pooling layer. Finally, the obtained data is flattened through the flatten layer and input into the full connection layer to realize regression prediction.

The network model is trained by signal forward transmission and error back propagation. The initialization network weight and offset value in forward transmission are random values, and the loss function used in back propagation is the mean square error function, as shown in equation (2):

\[ loss = \frac{1}{m} \sum_{i}^{m} \left( y_{\text{predict}} - y_{\text{real}} \right)^2 \]  

(2)

In equation (2), \(y_{\text{predict}}\) and \(y_{\text{real}}\) respectively represent the model predicted value and experimental measured value of the ith sample, a total of \(m\) samples. In the training process, the loss value is minimized by continuously adjusting the weight and offset value of each layer. Adam (adaptive motion estimation) algorithm is used as the optimizer to optimize and updates the model.

3. Results
The estimation of GFR belongs to the field of medical research. Such problems are often used the receiver operating characteristic curve (ROC curve) for numerical diagnosis and comparison of estimation. The accuracy were analyzed by bias, precision, coincidence rate and 95% consistency. Therefore, this experiment used the above methods as the evaluation criteria of the experimental results.

In addition to using the above performance indicators to compare the results of the CNN model and various estimation methods and analyze the comprehensive performance, we also analyzed the correlation between eGFR and mGFR. The correlation analysis of eGFR and mGFR shows that \(eGFR_{\text{CNN}}, eGFR_{\text{GRNN}}, eGFR_{\text{CG}}, eGFR_{\text{MDRD}}\) and \(eGFR_{\text{CKD-EPI}}\) with mGFR was positively correlated with mGFR.
(correlation coefficients were 0.844, 0.760, 0.704, 0.678, 0.760, P < 0.01). The broken line diagram of eGFR and mGFR estimated by each model and method is shown in Figure 1 below.

Table 4. CNN model parameter setting.

| network layer       | model parameter                                                                 |
|---------------------|----------------------------------------------------------------------------------|
| Input layer         | estimated GFR input data after preprocessing                                     |
| convolution layerC1 | in_channels=16,out_channels=1, stride=1                                          |
| Convolution layerC2 | in_channels=16, out_channels=1, stride=1                                         |
| Pooling layerS3     | Maxpooling=1                                                                     |
| Convolution layerC4 | in_channels=64, out_channels=1, stride=1                                         |
| Convolution layerC5 | in_channels=64, out_channels=1, stride=1                                         |
| Pooling layerS6     | Maxpooling=1                                                                     |
| Convolution layerC7 | in_channels=128, out_channels=1, stride=1                                        |
| Convolution layerC8 | in_channels=128, out_channels=1, stride=1                                        |
| Pooling layerS9     | Maxpooling=1                                                                     |
| Convolution layerC10| in_channels=64, out_channels=1, stride=1                                         |
| Convolution layerC11| in_channels=64, out_channels=1, stride=1                                         |
| Pooling layerS12    | Maxpooling=1                                                                     |
| Full connection layerF13 | 1 neuron                     |
| Output layer        | 1 neuron, output eGFR                                                            |
3.1. Comparison between CNN Model and Traditional Methods

The mGFR and eGFR calculated by CNN model and traditional equations have good correlation. In the early diagnosis of CKD, comparing the ROC and AUC of eGFR in each method, CNN was the largest, MDRD and CKD-EPI were the largest, and CG formula was the worst. The Youden index of the best node in CNN model was greater than CG, MDRD and CKD-EPI. The difference of each formula was statistically significant (P < 0.01). See Table 5.

In the comparison of various methods, the bias of CNN estimated by CNN model was less than that calculated by CG formula, MDRD formula and CKD-EPI formula. The precision of CNN model was higher than that of CG formula, MDRD formula and CKD-EPI formula. The coincidence rate of CNN model (including 15%, 30% and 50%) was higher than that of CG formula, MDRD formula and CKD-EPI formula. Compared with traditional statistical methods, CNN model had the best consistency effect. See Bland Altman consistency analysis diagram of each method in Table 6 and Figure 2.

Table 5. Comparison of GFR numerical efficiency of different methods.

| Methods  | eGFR/mL/(min·1.73m²) | R   | AUC | Critical value | Specificity | sensitivity | Youden index |
|----------|----------------------|-----|-----|----------------|-------------|-------------|--------------|
| CNN      | 79.88(65.73, 97.61)  | 0.844 | 0.950* | 70.9           | 0.142       | 0.958       | 0.858        |
| CG       | 85.31(58.40, 105.79) | 0.678 | 0.892* | 63.22          | 0.242       | 0.958       | 0.758        |
| MDRD     | 79.93(57.04, 95.07)  | 0.760 | 0.883* | 73.66          | 0.292       | 0.708       | 0.708        |
| CKD-EPI  | 81.48(60.58, 103.23) | 0.704 | 0.913* | 78395          | 0.292       | 0.708       | 0.708        |

Note: R: Pearson correlation coefficients of eGFR and mGFR, * p < 0.01, AUC: Compared with mGFR, * p < 0.01. Sensitivity, Specificity and Youden index are the corresponding values of the best node on the ROC curve.

Table 6. Comparison of deviation, coincidence rate and consistency between eGFR and mGFR.

| method(s) | B distribution / case | 15%mGF R coincidenc e rate/% | 30%mGF R coincidenc e rate/% | 50%mGF R coincidenc e rate/% | eGFR and mGFR consistency |
|-----------|-----------------------|--------------------------------|-------------------------------|-------------------------------|---------------------------|
|           |                       |                                |                               |                               |                           |

Figure 1. Comparison of estimation results of each.
3.2. Comparison between CNN Model and GRNN Model

The eGFR and mGFR estimated by CNN model and GRNN model have good correlation. In the early diagnosis of CKD, the ROC and AUC of eGFR of the two models were compared. CNN model was greater than GRNN model. The Youden index of the best node of CNN model was greater than that of GRNN model. The differences among models was statistically significant ($P < 0.01$). See Table 7.

Table 7. Comparison of numerical efficiency of GFR estimated by CNN and GRNN.

| methods | eGFR/mL/(min∙1.73m²) | R   | AUC | Critical value | Specificity | Sensitivity | Youden index |
|---------|-----------------------|-----|-----|----------------|-------------|-------------|--------------|
| CNN     | 79.88 (65.73, 97.61)  | 0.844* | 0.950* | 70.9 | 0.142 | 0.958 | 0.858 |
| GRNN    | 81.94 (66.73, 96.87)  | 0.760* | 0.873* | 70.905 | 0.383 | 0.917 | 0.617 |

Note: R: Pearson correlation coefficients of eGFR and mGFR, * $p < 0.01$, AUC: Compared with mGFR, * $p < 0.01$. Sensitivity, Specificity and Youden index are the corresponding values of the best node on the ROC curve.

In the comparison of the two models, the bias estimated by CNN model was less than that of GRNN model. The precision result of CNN model was higher than that of GRNN model. The coincidence rate of CNN model (including 15%, 30% and 50%) was higher than that of GRNN model. Compared with GRNN model, CNN model has the best consistency effect. See Bland Altman consistency analysis diagram of each method in Table 8 and Figure 2.

Table 8. Comparison of deviation, coincidence rate and consistency between eGFR and mGFR.

| Method | B | P | 15%mGFR R coincidence rate% | 30%mGFR R coincidence rate% | 50%mGFR R coincidence rate% | B distribution / case | eGFR and mGFR consistency |
|--------|---|---|-----------------------------|-----------------------------|-----------------------------|------------------------|---------------------------|
| CNN    | 0.9 | 7 | 22.0 | 35.29 | 61.76 | 88.24 | 17 | 17 | -44.2-42.3 |
| GRNN   | 3.0 | 3 | 26.2 | 26.47 | 58.82 | 82.35 | 20 | 14 | -54.6-48.5 |

Note: R: Pearson correlation coefficients of eGFR and mGFR, * $p < 0.01$, AUC: Compared with mGFR. Sensitivity, Specificity and Youden index are the corresponding values of the best node on the ROC curve.
4. Discussion

GFR is the main parameter to evaluate renal function and the main basis for CKD stage. However, there is no direct and effective measurement for GFR value. Although there are many equations that can calculate GFR at home and abroad, these equations were first started abroad and calculated based on the data of Europeans and Americans. Although the calculations of Asians have been revised, an equation that can be calculated accurately has not been found. After the rise of big data, deep learning was introduced to precisely calculate GFR with the help of artificial intelligence.

This experiment does not optimize and adjust the neural network model that has been applied to estimate GFR, such as BP neural network, RBF neural network, generalized regression neural network, etc; Instead, a model based on convolutional neural network is proposed. In this experiment, CG equation, MDRD equation, CKD-EPI equation and generalized regression neural network model which have great advantages in calculating GFR in Chinese are compared with CNN to verify that convolutional neural network can be applied to estimate GFR and has better results.

Although the experimental results are good, there are still some deficiencies in the experiment. First, the sample size is relative small. This study only analyzes and compares the results of the training set, and does not further analyze the application of CNN model in each stage of CKD. Second, the variables such as urea nitrogen, serum creatinine and cystatin C used need to be obtained by laboratory methods. The standard mGFR is measured by renal dynamic imaging. These methods may have some errors.

5. Conclusion

The main content of this paper is to propose a convolution neural network model to estimate GFR. Through the comparison of a series of performance indexes such as efficiency, bias, precision, coincidence rate and consistency, it is proved that CNN model can be applied to estimate GFR and is better than GRNN neural network.

But the data set of the study is relatively small, and the stage of the data obtained is poor. In the future, we will continue to collect case data of CKD patients, further expand the data set, continue to improve research, and develop a GFR estimation model that is more suitable for the Chinese.
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