A Meta-analysis on diagnostic value of serum cystatin C and creatinine for the evaluation of glomerular filtration function in renal transplant patients

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Abstract:

Objectives: This meta-analysis aimed to perform a systematic review on comparing the diagnostic value of serum cystatin C and creatinine for glomerular filtration rate in renal transplant patients.

Methods: The data was extracted into 2×2 table after the articles were assessed by the tool of QUADAS and heterogeneity analysis. The SROC curve and meta-analysis were performed by MetaDisc1.4.

Results: Meta-analysis showed that the serum cystatin C had no heterogeneity (P=0.418, I2=2.2%, DOR=25.03), while creatinine heterogeneity was high (P=0.109, I2=37.5%, DOR=9.11). The values of SEN, SPE and SAUC were calculated as 0.86, 0.70 and 0.9015 for cystatin C , and 0.78, 0.73 and 0.8285 for creatinine individually. This study utilized GFR detection and subgroups analysis by cutoff. The PLR was 6.13 and the NLR was 0.12 for cystatin C , compared to SCr (3.72, 0.32). There was homogeneity among these studies using PENIA testing for cystatin C ($\chi 2$=2.61, P=0.4560, I2=0.0%.

Conclusions: There were significant correlations among cystatin C , creatinine and glomerular filtration rate (GFR). Cystatin C had more sensitivity but less specificity than creatinine for evaluation of GFR. Cystatin C had strong ability in diagnosing renal function after renal transplant and ruling out diagnostic efficacy.

Key words: Cystatin C; creatinine; renal transplantation; glomerular filtration rate; meta-analysis.

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Introduction

The accurate and timely assessment of renal function in patients after renal transplant was provided with great important clinical significance[1]. The glomerular filtration rate (GFR) as an important renal function indicator was measured by the gold standard method for determination the clearance rate of exogenous markers, such as inulin, iohexol, 125I-iothalamate, 99mTc-DTPA, 51Cr-EDTA and other radioactive materials[2]. But these methods which are cumbersome, time consuming and have significant potential side effects were generally used for scientific research or clinical trials with higher professiona[13].

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The endogenous indicators including serum creatinine and endogenous creatinine clearance rate were usually used to assess GFR in clinically. However, the generation of creatinine was effected by age, sex, muscle mass, drug use and other factors. Moreover, tubular secretion and visceral additional clearance resulted in the concentration of serum creatinine within the reference range[4] when the renal function loss reached 50%. Therefore, serum creatinine showed low sensitivity in the diagnosis of renal failure after kidney transplantation, especially in some minor aspects of renal impairment, children, the elderly and other special patient population[3,5].

In recent years, serum cystatin C as an ideal endogenous marker had been progressively concerned in the evaluation of GFR function. Numerous studies showed[6,7] that cystatin C as a serum marker was more sensitive than serum creatinine in reflecting GFR. cystatin C was generated at a constant rate by the nucleated cells of organism, and could freely get through glomerulus and get completely decomposed after reabsorption in the proximal tubule epithelial cells but it didn't get back to the blood and couldn't secreted by renal tubular. In ad-

dition, the characteristics of serum cystatin C were very close to the required characteristics of the ideal GFR endogenous target. The contents of serum cystatin C were relatively stable and not affected by any external factors. It was reported[8] that cystatin C , with a positive charge, had greater molecular weight than creatinine . So it was easier to reflect the changes of early glomerular filtration membrane permeability. And cystatin C, with smaller differences between individuals, increased when GFR had slight decrease. It possessed more prominent clinical significance in the monitoring of renal function in patients with renal transplant. This study was on the basis of domestic and foreign researches before January 2013, and discussed the diagnostic value of cystatin C and creatinine for GFR after renal transplantation, anticipating to provide an evidence for base medicine.

Materials and methods

Literature inclusion and exclusion criteria

The object of study

The kidney transplant recipients, including children and elderly patients, whose primary disease covering the whole spectrum of disease before transplantation had been studied. The cut-off value of GFR was great than 30mL/min in experimental detection.

Type of Study

Direct comparison of cystatin C with creatinine had been detected on the diagnostic tests of GFR diagnostic value, based on cross-sectional studies, the pattern of cohort studies and case-control studies. The relevant literatures compared cystatin C with the result of serum creatinine based formula of MDRD / Cockcroft and Gault (CG) formula, or based on the formula results of cystatin C, creatinine were excluded in this study.

GFR was the critical reference standard in the evaluation of renal function after kidney transplantation. The test method for GFR was gold standard, also known as the clearance rate of exogenous markers, including ulin, iohexol, 125I-iothalamate, 99mTc-DTPA, 51Cr-EDTA and so on. Besides, 24h-urine creatinine clearance could act as a reference method according to the concrete implement of the test.

In the detection of cystatin C and creatinine , all of clinical methods should be included. The detection method of cystatin C contained the particle-enhanced turbidimetric immunoassay (PETIA) and particle- enhanced nephelometric Immunoassay (PENIA). Jaffe method and enzymatic had used for creatinine detection.

Measurement index

The summary sensitivity (SEN), summary specificity (SPE), summary positive and negative predictive values (±PVs), summary positive and negative likelihood ratios (±LRs), diagnostic tests combined odds ratio (DOR), area under the summary receiver operating characteristic (SROC). The literatures , which couldn't extract the fourfold table (TP, FP, TN, FN), had been excluded.

Literature Search Strategy

This study mainly conducted a systematic literature search of the PubMed (http://www.ncbi.nlm.nih.gov/pubmed/) through 1985 to December 2012, and the Cochrane Library (http://www.thecochranelibrary.com/view/0/index.html) databases at 2012 No. 4 by using the following keywords: cystatin C, Creatinine, renal transplant, GFR, diagnosis test, sensitivity, specificity and the like. The same keywords were used to retrieve from Chinese Academic Journal and Chinese Biomedical Literature database during 1985 to January 2013. Using the combination of subject terms and keywords, the supplement search was carried out through Google Scholar and other search engines on the Internet. Meanwhile, the references of the literatures had been tracked for the secondary search until any new requirement documents were no longer found. We would contact with the author by e-mail if test reports were not in detail or lack of information.

Literature screening and data acquisition

The study excluded reviews, personal views and secondary published literature in the way of reading the abstracts. In addition, the diagnostic study including diagnostic studies, extracted population characteristics, total number of cases, the cut-off value, true positive, false positive, true negative and false negative data was extracted from the text that possessed fourfold table data by reading context. On this foundation, quality analysis was carried out according to evaluation criteria. Two investigators independently conducted the literature screening and quality assessment according to the literature inclusion and exclusion criteria, then cross-checked. Discrepancies were resolved via compromise settlement or discussion with a third person.

Literature quality assessment

The quality evaluation criteria were performed in accordance with QUADAS system described by Whiting P, etc. Evaluation criteria consist of six components:1 whether to include all kinds of cases and easy confusion illnesses;2 whether the selection criteria and characteristics of the study was clear;3 could the gold standard correctly classify the disease status;4 whether all cases, regardless of the index test results, had examined with the same gold standard;5 whether the implementation of the evaluation tests were described in detail;6 did the test results include all the cases which participate in the study .

Meta-analysis

Meta-analysis was carried out by MetaDisc 1.4 software. The literature was summarized as SEN, SPE, ±PVs,±LRs OR for diagnostic tests, and analyzed the heterogeneity among each study with $\chi 2$ test. If there was absence of statistical heterogeneity among each study [P> 0.10, variance ratio (I2) <50%], Meta-analysis was performed using a fixed-effects model (FEM). Otherwise, random effects models (REM) would be used to analyze the possible causes of heterogeneity and subgroup analysis further. At last, this study should draw the (SROC) curve based on the including literatures and calculate the area under the receiver operating characteristic curves(SAUC). All the results were indicated with 95% confidence interval (CI).

Analysis of summary measurement index

Summary measurement index was visually displayed through drawing the forest diagram form.

Subgroup analysis

Uniform gold standard method of GFR, cut-off values, P values of cystatin C and Cr test method were calculated and then conducted Meta-regression analysis to acquire the main source of heterogeneity and subgroup analysis. The summary ±PV was as the main evaluating indicator.

SROC analysis

SROC curve was drawn via Moses-Littenberg regression model[12]. All data was calculated as follows:

D=logit(TPR)−logit(FPR) S=logit(TPR)+logit(FPR)

$$\square \quad Sen \quad 1\square Spe\square$$

$$\square D=\log DOR,\ S=\ln\square \frac{\quad}{Spe}\square,\ \text{TPR= True positive rate, FPR= False positive rate})$$
$$\square 1\square Sen$$

The ideal formula of the curve was D= a + bS, D represented the accuracy of a waiting for evaluation index, S represented the threshold effect of the data. b=0, there was absence of heterogeneity and SROC curve was symmetrical curve; b≠0, SROC was asymmetric curve. The relationship of a and b as follows:

$$Sen=\left[1+e^{-a/(1-b)\left(\frac{Spe}{1\square Spe}\right)^{(1+b)/(1-b)}}\right]^{-1}$$

Results

The characteristics of literatures

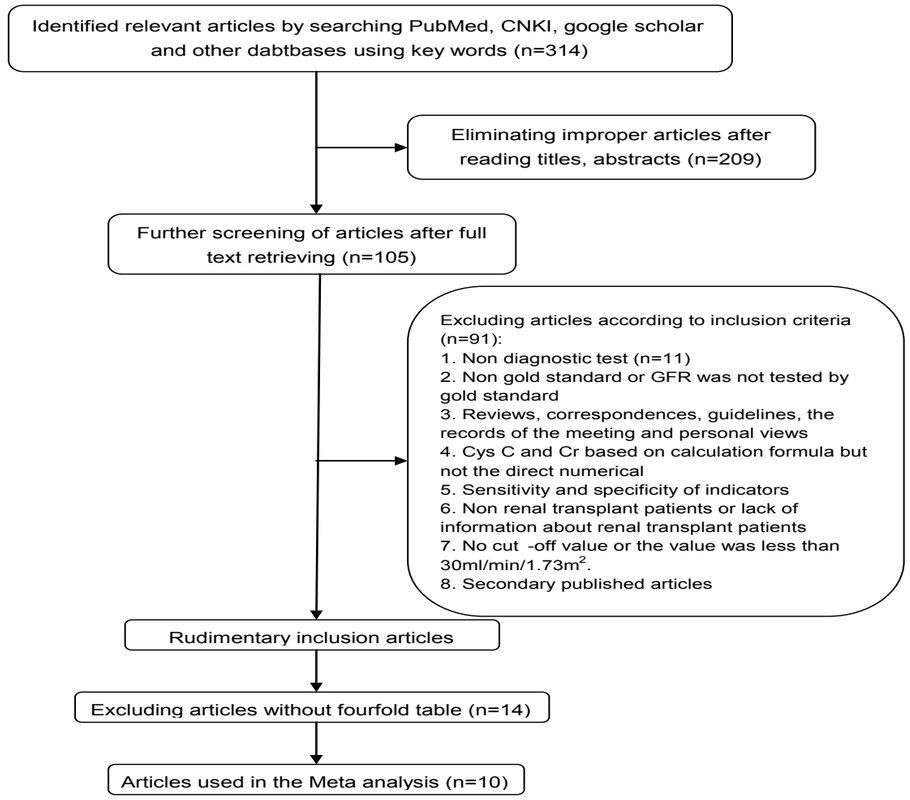
Literature search and screening

The flowchart of literature search and screening was shown in Fig 1. The initial literatures search identified 314 studies. Of these, 105 were excluded after reading text titles and abstracts, and only 24 literatures met the inclusion criteria. We contacted three authors of the 24 literatures, in order to obtain the details of the fourfold table and some incomplete information, but didn't get a reply. Finally, 14 literature sources were excluded due to the insufficient fourfold table data, and merely 10 literature sources served as the research literatures. Among the rest, 7 literature sources were in English, and 3 were in Chinese. All the studies were about diagnostic test of GFR value via cystatin C and creatinine .

The basic information of included studies

10 literature sources and 692 cases of renal transplant recipients had been adopted in this study, excluding children and elderly patients, as a whole the men slightly more than women. 2 literature sources reported the situation of the disease after renal transplantation. For the cut-off value of the evaluation of the renal function, the values of cystatin C and creatinine were 1.07 ~ 1.64 mg /

Fig. 1 Study selection process. / Flowchart of publication selection.



L and 106.1 ~ 130.7μmol / L, respectively. And other 2 literature sources didn't mention these indicators. The cut-off value of GFR tested by gold standard was 80 ml/min/1.73m2 (60~90 mL/min/1.73m2). The detection methods of GFR included ulin, iohexol, 125I-iothalamate, 99mTc-DTPA and endogenous 24h CrCl.

Simultaneously, the detection method of cystatin C contained PETIA and PENIA., while Jaffe method and enzymatic had used for creatinine detection. The main characteristics of the literatures were shown in Table 1 and Table 2.

Table 1 The basic situation of the adopted literature

Study	Country	NO. of patients	Average	Male(%)	The use of	The cut-	Normative
Lorenz Risch 1999[16]	Switzerland	30	49±15.5	50% (15/30)	Cyclosporin A + Prednisone	60	^{125}I-iothalamate
Jean-Philippe Daniel 2004[13]	France	103/6	40.4±11	35%	Cyclosporin A+	6	Inul
Fu Keung Li 2002[14]	Hong Kong, China	10 6	38.5±7.5 (5	50	Prednisone+ Azathioprin Cyclosporin A	80	Cr Cl
E. Paskalev 2001 [17]	Bulgaria	4	51±14	50	Imuran+Pre	6	Cr
Daihong Li 2010 [20]	Tianjin, China	5	44.3±13	41.4	Tacrolimus+ Mofetil+	9	^{99m}Tc-DTPA
Junsheng Ye 2010 [21]	Guangdong, China	7	41.8±13	65.7	Glucocortic Mycophenol P	6	^{99m}Tc-DTPA
Fupu Zheng 2005 [22]	Guangdong, China	2	45±20	60.9	r e d	80	^{99m}Tc-DTPA
N.Krishnamurthy. K 2011[19]	India	30	43.13±10	73.3% (22/		60	^{99m}Tc-DTPA
Stefan Herget-Rosenthal 2000[15]	Germany	1	49±14	51.8	Cyclosporin Azathioprin T	8	Cr

Table 2 The fourfold table data of the adopted literature

Study	Serum Creatinine						Cystatin C					
	Detection method	Cut-off	TP	FP	TN	FN	Detection method	Cut-off value	TP	FP	TN	FN
Lorenz Risch	PETI	1	15	1	8	6	Reform met	12	1	5	4	4
Jean-Philippe Daniel	Dade Behring	1	26	8	2	5	hod	130.74	2	1	50	17
Fu Keung Li	Latex Cys C assay	1	68	8	2	5	Reform	12	5	1	20	21
E. Paskalev 2001	Latex Cys C assay	1	19	2	1	6	met hod	12	2	9	6	5
Daihong Li 2010	PETI	N	26	6	2	3	met hod	N	2	9	20	4
Junsheng Ye 2010 [21]	PETI A	1.5	17	4	4 6	3	Jaff method	12 5	1 9	4	40	7
Fupu Zheng 2005 [22]	Dade Behring N	1.0	16	0	6	1	Jaff method	11 8	1 2	1	5	5
N.Krishnamurthy. K 2011[19]	Latex Cys C assay PETI A	1.2	16	1	1 2	1	Jaff method	106.1	1 4	6	8	3
Christensson A 2003 [18]	PETI A	NA	98	5	13	9	Enzymic method	NA	8 3	4	24	14
Stefan Herget-Rosenthal 2000[15]	Dade Behring N	1.3	25	5 8	2 6	1	Reform Jaffe	106.8	2 2	2 8	56	4
	Latex Cys C						method					

Dade Behring N Latex Cys C assay was one of the PENIA, NA, Non data acquisition

The quality assessment of the adopted literature sources

The quality assessment of diagnostic accuracy studie (QUADAS) was shown in Table 3. All adopted literature sources were not mentioning the blinded method, and most of them didn't list the diseases foundation of the observed objects. Therefore these studies were deemed incomplete and confusing cases. Furthermore, major literature sources also didn't mention the situations of withdrawals or whether all of the data were included in the calculation. In general, the quality of the adopted literature sources was higher.

Table 3 The QUADAS of the adopted literature

Study	Type of test	Disease spectrum	Selection	Golden standard	Multiple	Implementation of	Lost of follow up
Lorenz Risch 1999[16]	Cohort study	N O	YES	YES	YES S	YES S	YES S
Jean-Philippe Daniel 2004[13]	Cohort study	N O	YES S	YES	YES S	YES S	YES S
Fu Keung Li 2002[14]	Cohort study	Y E	YES S	NO	YES S	YES S	NOT CLEAR
E. Paskalev 2001 [17]	Cohort study	Y E	YES S	NO	YES S	YES S	NOT CLEAR
Daihong Li 2010 [20]	Cohort study	N O	YES S	YES	YES S	YES S	NOT CLEAR
Junsheng Ye 2010 [21]	Cohort study	N O	YES S	YES	YES S	YES S	NOT CLEAR
Fupu Zheng 2005 [22]	Case-control study	N O	YES S	YES	YES S	YES S	N O
N.Krishnamurthy. K 2011[19]	Case-control study	N O	YES S	YES	YES S	YES S	NOT CLEAR
Christensson A 2003 Stefan Herget-Rosenthal 2000[15]	Cohort study	N E	YES S	YES	YES S	YES S	NOT CLEAR

Note: Disease spectrum composition means that whether include the various cases or confusion of illness.

The results of Meta-analysis

Heterogeneity analysis

10 summary OR (95% CI) and heterogeneity analysis values of independent studies were shown in Fig 2A and Fig 2B.

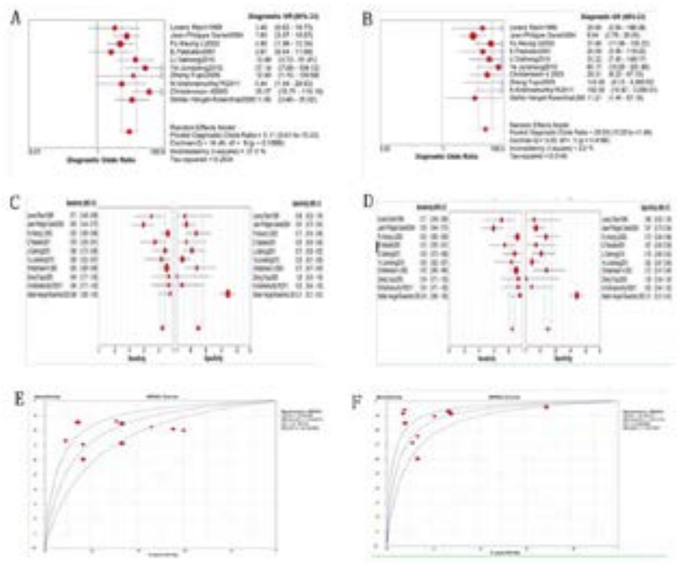


Fig. 2 Meta-analysis on diagnostic value of the creatinine and cystatin C. A,B Forest plots for summary OR and heterogeneity analysis of the creatinine and cystatin C detection; C,D Forest plots for summary SEN and SPE of the creatinine and cystatin C; E,F The SROC curve of creatinine and cystatin C assessment on GFR after renal transplantation.

Calculated results of a random effects

model demonstrated that the DOR value of cystatin C was greater than that of creatinine , but their CI showed the fraction overlap. In addition, the calculation of the spearman correlation coefficient between sensitivity logarithmic and 1-specificity logarithm showed that cystatin C=0.213 (P = 0.555), and Cr= 0.140 (P = 0.699). The result inferred that weak correlation existed in logarithmic of sensitivity and 1–specificity, and it was little possibility that a threshold effect leaded to the heterogeneity. Moreover, the diagnostic studies of both cystatin C and creatinine were I2 < 50%, and cystatin C had a smaller I2 value. The results showed that heterogeneity were resultd from a non-threshold effect existed among the adopting literatures.

Summary effect size

In 10 independent studies, the summary SEN and SPE (95% CI) of creatinine and cystatin C were shown in Fig 2C&2D and Table 4. Forest map intuitively showed that the specificity of cystatin C had significant heterogeneity ($\chi2 = 91.88$, $I2 = 90.2\%$). And the result of summary effect size showed that the SEN of cystatin C was much higher and the SPE was similar to creatinine.

Table 4. The data of forest plots for pooled sensitiveness and specificity of the Cr and Cys C

	Cr		Cys C	
	sensitivity	specificity	sensitivity	specificity
Merge value（95%*CI*）	0.78（0.73-0.82）	0.73（0.68-0.78）	0.86（0.82-0.90）	0.70（0.65-0.75）
χ^2 teat value（*P* value）	15.25（0.0844）	30.43（0.0004）	34.27（0.0001）	91.88（0.0000）
I^2 value	41.0%	70.4%	73.7%	90.2%

SROC curve

10 SROC curve of the diagnostic value of GFR after renal transplantation via cystatin C and creatinine were shown in Fig 2E&2F. The splashes of cystatin C and creatinine showed the non-scatter "shoulder arm" shape, and there was less possible of threshold effect in the inclusion literatures. Furthermore, compared with the AUC of creatinine, that of the cystatin C was greater (AUCCr = 0.8285, AUCcystatin C=0.9015), which demontrated the diagnostic accuracy was higher.

Subgroup analysis

Most guidelines recommended that the diagnostic criteria for renal function after kidney transplantation was GFR≤80 mL/min/1.73m², but the range of GFR cut-off values in the inclusion literatures was from 60 to 90 mLl/min/1.73m². In addition, the Meta-regression analysisshowed that the major source of heterogeneity was different from the reference standards of GFR test. Therefore, in the subgroup analysis, the detection reference standards based on the cut-off value ≤80 mL/min/1.73m² of GFR and 99mTc-DTPA as the limited conditions. Three groups (n= 123) as the subjects were selected and shown as merger of positive and negative likelihood ratio (DLRs) in Table 5. Comparing the degree of heterogeneity, the merged positive likelihood ratio of cystatin C($\chi2=3.99$,P=0.1357)and creatinine($\chi2=7.83$,P=0.0199) was more obvious. The merged negative likelihood ratio of that was unconspicuous and the values were $\chi2=0.54$, P=0.7635 for cystatin C and $\chi2=0.12$, P=0.9408 for creatinine respectively.

Table 5 Subgroup analysis of Cys C and Cr

The detection standard of the GFR was ^{99m}Tc-DTPA and cut-off value≤80 mL/min/1.73m^2,

Diadynamic criteria Merge likelihood ratio (LRs) Heterogeneity test (P value)

	PLR (95%CI)	NLR(95%CI)	PLR	NLR
Cys C	6.13（2.38-15.79）	0.12（0.07-0.21）	*P*=0.1357	*P*=0.7635

（4.88-11.88），SEN=0.75，SPE=0.72，Only 1 piece using enzymatic.

In this study, a subgroup analysis was also conducted in the different methods of Cys C and creatinine. Among the adopted literature sources, there were 4 that detected cystatin C using PETIA, and the results were 0.4560, I^2=0.0%, DOR=37.63（11.68-121.26），SEN=0.83，SPE=0.91. 6 ones ployed PENIA and the results were *P*=0.3024，I^2=17.2%，DOR=23.56（12.93-94），SEN=0.87，SPE=0.67. Then 9 ones used modified Jaffe to assay the value Cr (*P*=0.3661，I^2=8.3%，DOR=7.61).

Discussion

Most patients may have an acute and chronic rejection or complications of chronic allograft nephropathy after kidney transplantation, and early diagnosis and treatment of renal injury will directly affect the prognosis of patients. Hence the goal of clinical research is to look for an early, sensitive, specific indicator of GFR. Previous research[23] suggested the ideal endogenous indexes of GFR should maintain a constant ratio in serum or plasma, and it can pass freely through glomerular filtration membrane. It cannot be reabsorbed by renal tubular, and secreted by renal tubular, and there is no extra renal elimination. Serum creatinine is the most commonly used evaluation index of renal function, though there are many limitations, but it still plays an important role in clinic. The research about judging the damage of renal function found that cystatin C is also a kind of ideal index reflecting the endogenous change of GFR. In this study, Meta-analysis is carried out through 10 articles to study the diagnostic value of GFR after kidney transplantation in a systematic way.

The results of meta-analysis showed that the Diagnostic OR of cystatin C and creatinine have a good correlation with GFR, but there is a small overlap in 95% confidence interval of DOR, thus the difference is not significant. cystatin C diagnosis research has no obvious heterogeneity (P = 0.4186, I2 = 2.2%), and creatinine diagnosis has obvious heterogeneity (P = 0.1089, I2 = 37.5%).In these studies, GFR diagnosis sensitivity of cystatin C is higher than Cr after kidney transplantation (SENCys C=0.86, SENCr=0.78); but the specificity is lower than creatinine(SPECys C=0.70, SPE creatinine =0.73).This conclusion is also confirmed through the SAUC(AUCCr=0.8285, AUCCys C=0.9015). AUC or the correlation co-efficient was used as a diagnostic performance evaluation index alone in many past studies[24-26], but this study takes the quality of literature, literature of heterogeneity and GFR, cystatin C, creatinine cutoff value into consideration, and SEN -SPE evaluation effectiveness has more clinical significance.

From the forest plots for the degree of SEN and SPE, the summary effect of the cystatin C and the creatinine value have obvious heterogeneity. When analyzing the sources of heterogeneity, five different methods of standard were used to research GFR detection, and the cutoff value is also different.Therefore this study conducted a subgroup analysis after limiting the GFR (99 MTC - DTPA) test method and the cutoff value (80 mL/min / 1.73 m2 or less). Evidence including three research groups (n = 123) indicates the likelihood ratio of cystatin C range is bigger (PLR = 6.13, NLR = 6.13) than creatinine (PLR = 3.72, NLR = 3.72). Therefore the likelihood ratio of cystatin C has stronger ability to diagnose renal injury after renal transplantation and exclude diagnosis effectiveness. However, in the subgroup analysis, the positive likelihood ratio of the cystatin C and creatinine still has the obvious heterogeneity, This shows that because of different calculation methods, different population constitution, GFR measure by radioactive nuclide material has some problems in the detection accuracy, repeatability. The heterogeneity of the negative likelihood ratio of the cystatin C and creatinine can be ignored because there is no obvious heterogeneity.

The sub group analysis of cystatin C and creatinine showed that a significant rise in P values. It indicated that heterogeneity was associated with detection method. The reagents of PETIA were mostly bought from Dako company, but PENIA mainly used the reagents of Behring company. The Jaffe method was usually used for the test of creatinine, and some research using the improved Jaffe method. Different instruments, reagents, calibration, calculation and reference range and cutoff values led to the differences between different methods.

The research had a limitation that the composed information of disease spectrum in patients including in the research is not complete. The information excludes the various chronic kidney diseases after renal transplantation (eg. nephropathy of recurrent IgA, nephrotoxicity nephropathy of cyclosporine A, focal glomerulosclerosis, acute exacerbation of chronic allograft nephropathy and so on) and the easily confused diseases (eg. Transplanted glomerulonephritis etc.), which existed clinical heterogeneity. For example, E.Paskalev found that the hyperfiltration condition was easy to appear in the long-term follow-up process of transplanted renal in the patients with diabetic nephropathy which accounted for 15% of underlying diseases. The concentration of serum creatinine C decreased rapidly. However, it could not represent all the progression of nephropathy after chronic kidney transplantation3. In addition, the detection time of evaluation indexes was various, and it couldn't exclude the effect of the state of progression of transplanted renal on experimental results, which would increase the heterogeneity of study.

The research also analyzed the influence of immunosuppressants on the detection of cystatin C and Cr after renal transplantation. Bokenkamp. A[27] indicated that the concentration of cystatin C in children's serum after renal transplantation was higher than other kidney diseases in children. Risch and L etc.[28] confirmed that cyclosporin A and prednisone had non-significant effect on the concentrations of cystatin C. However, cystatin C could generate extensively and increase dose-dependence using dexamethasone in HeLa cell in the vitro. The application of the immune suppressive agents in the literature of this research was almost the same and the effect of this factor on the result couldn't be observed, therefore it requires further research.

In recent years, the formulas based on cystatin C and creatinine were used for predicting GFR in clinical studies to increase daily[29]. The formulas counted ethnic, sex, age and other factors and made it more accurate for the evaluation of GFR. Min Z etc[30]. Demonstrated significant correlations between cystatin C, SCr and GFR. cystatin C was more sensitive, but less specific, than serum creatinine for the estimation of GFR in patients with chronic kidney disease. Moreover, one literature31 about the diagnostic value of GFR after renal transplantation compared the diagnostic value via cystatin C with that of the MDRD formulas on the ground of creatinine after renal transplant. 105 cases of renal transplant recipients were brought into the research, and the average age of them was 49.5. The result showed that the cystatin C had more higher sensitivity (SENCys C=92.2%, SENCr=82.2%) and had same specificity (SPECys C=SPECr=93.3%) when GFR used both the standard method 99mTc-DTPA and the value of cut-off was 60 mL/min/1.73m2.

Conclusion

This study was aiming at the diagnostic value of cystatin C and creatinine after renal transplantation, and performed a systematic evaluation and Meta-analysis via retrieving domestic and foreign researches. According to the analysis results, the conclusions were as follows:

(1) cystatin C and creatinine showed a good correlation with GFR. The diagnostic sensitivity of cystatin C was higher than that of creatinine in patients after kidney transplant, but the specificity of cystatin C was shown lower than creatinine.

(2) When the detection method of GFR was limited to 99mTc-DTPA and the value of cut-off ≤ 80mL/min/1.73 m2, cystatin C had a larger range of likelihood ratio and stronger capacity for diagnosis of renal function after kidney transplant and exclusion diagnostic efficacy.

(3) The difference of detection methods between cystatin C and creatinine had great influence on heterogeneity.

Conflict of interest

The authors have no financial conflicts of interest.

Multiple reference bias means that whether all the cases of line was tested by the same golden standern. Lost of follow up bias means that whether the results contant all the cases of line.

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