ORIGINAL ARTICLE

Urinary Myeloperoxidase to Creatinine Ratio as a New Marker for Diagnosis of Urinary Tract Infection

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Key words: urine; myeloperoxidase; diagnosis; urinary tract infection

Objective To determine whether urinary myeloperoxidase to creatinine ratio (MCR) can serve as a marker for diagnosis of urinary tract infection (UTI).

Methods Patients suspected of UTI were consecutively enrolled and further divided into the culture positive and the sterile groups according to urine culture results. Subsequently, MCR, white blood cell (WBC) and bacteria in the urinary samples from patients were detected and compared between the two groups.

Results Finally, 253 patients were enrolled including 157 urine culture positive patients and 96 urine culture negative patients (sterile group). After logarithmic transformation in 2 as the base, the MCR, WBC, and bacteria were separately presented as $\log_2^{\text{MCR}}$, $\log_2^{\text{WBC}}$ (quantitative), and $\log_2^{\text{bacteria}}$. The values of $\log_2^{\text{MCR}}$ (8.6 ± 2.5 vs. 5.4 ± 1.5 , $t = -12.453$, $P = 0.001$), $\log_2^{\text{WBC}}$ (quantitative) (8.0 ± 2.5 vs. 5.2 ± 1.8 , $t = -10.332$, $P = 0.001$), $\log_2^{\text{bacteria}}$ (11.4 ± 2.5 vs. 8.2 ± 2.8 , $t = -9.297$, $P = 0.001$) and WBC (semi-quantitative) [2 (interquartile range 1, 3) vs. 1 (interquartile range 0.5, 1), $Z = -7.580$, $P = 0.001$] showed significant difference between the urine culture positive group and the sterile group. Among the urine culture positive group, the values of $\log_2^{\text{MCR}}$ of the gram positive and gram negative subgroups were 7.2 ± 2.5 and 9.0 ± 2.4 ($t = 4.016$, $P = 0.001$), respectively. The correlation between $\log_2^{\text{MCR}}$ and $\log_2^{\text{WBC}}$ (quantitative), $\log_2^{\text{bacteria}}$, WBC (semi-quantitative) was 0.708 (Pearson correlation, $P = 0.001$), 0.381 (Pearson correlation, $P = 0.001$), and 0.606 (Spearman correlation, $P = 0.001$), respectively.

Conclusions MCR is positively correlated with WBC counts and could be served as a promising biomarker for diagnosis of UTI. MCR could be even used for initial inference of infectious bacteria types of UTI.

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URINARY tract infection (UTI) is the most common bacterial infectious diseases encountered in clinical practice.¹ Patients with UTI usually presents with dysuria, urinary frequency and urgency.²⁻³ Many complications including dehydration, sepsis, kidney failure can occur in patients with UTI,⁴ nevertheless, if treated early and adequately, the prognosis is good for most patients.⁵⁻⁶

UTI is diagnosed based on suspected infection symptoms, urinary routine test, and urine culture and so on. However, diagnosis of UTI is complex because older people do not always exhibit the signs and symptoms commonly associated with UTI.⁷ Dipstick urinalysis is popular for its availability and usefulness, but results must be interpreted in context of the patient's pretest probability based on symptoms and characteristics.⁸ Demilie *et al*⁹ demonstrated that the use of dipstick urinalysis for screening UTI particularly asymptomatic bacteriuria yielded the significantly false positive and negative diagnostic results when compared against the gold standard culture method, which is consistent with the results reported by Masinde *et al*.¹⁰ Although quantitative urine culture is the gold standard method for UTI diagnosis, it is labor-intensive and time consuming.¹¹ In recent years, several urinary biomarkers, such as xanthine oxidase, myeloperoxidase (MPO) and neutrophil gelatinase-associated lipocalin have been proved to be useful for early detection of UTI,^{5, 12-15} among of which, the sensitivity, specificity, positive predictive value, and negative predictive value of MPO for detection of UTI were 87%, 100%, 100%, and 94%, respectively.⁵ MPO, an abundant heme protein secreted from activated phagocytes,¹⁶ which holds a central role in microbial killing in humans and animals.⁵ MPO catalyzes hydrogen peroxide mediated peroxidation of halide ions and pseudohalide thiocyanate, which are responsible for killing phagocytized bacteria and viruses.¹⁷

Although Ciragil *et al*'s study⁵ has demonstrated that urinary MPO may be a new marker in early detection of UTI, we think there are still some problems that need to be solved. Firstly, they did not ruled out the possibility of MPO leakage from blood to urine which may be attributed to the destruction of glomerular basement membrane. Secondly, they did not compare the efficacy of MPO *versus* other indicators in diagnosis of UTI. Thirdly, MPO level between the gram positive and negative subgroups was not compared for the urine culture positive group. Therefore, this study

aimed to assess the possibility of MPO for diagnosis of UTI by (1) comparing urinary MPO level between the urinary culture positive and negative groups, (2) comparing the capacity of urinary MPO for UTI diagnosis with other indicators, such as white blood cell (WBC) and bacteria, and (3) comparing urinary MPO level of gram positive subjects with gram negative subjects.

PATIENTS AND METHODS

Patients enrollment and sample collection

A total of 328 outpatients clinically suspected of UTI were consecutively enrolled in the present study between December 2015 and January 2017. The patients presented with dysuria, frequency, urgency and abdominal/flank pain with or without fever. All the patients enrolled met the following two criteria: urinary protein test with dipsticks was negative and estimated glomerular filtration rate (eGFR) was no less than 90 ml/(min·1.73 m²).¹⁸ Those who had received antibiotic therapy within two weeks were excluded from the study.

The study was approved by the ethics committee of the Aerospace Central Hospital. All the participants agreed to the study and signed informed consents.

The clean-catch midstream urinary specimens were collected with sterile plastic containers and divided into three parts: one for routine urine test within 30 minutes, another for microbiologic culture within 60 minutes and the last one was stored at -80°C in refrigerator for further biochemical analyses.

Urinary routine test

Urinary routine test consists of two parts. Urinary protein and WBC were semi-quantitatively determined on a urinary dipsticks analyser (Clinitek Advantus). In order to facilitate statistical analysis, the semi-quantitative results provide a grade estimate for protein and WBC count in urine comprising five ordinal grades (-, ±, +, ++, +++), where grade - is assigned a value of 0, grade ± is assigned a value of 0.5, grade + is assigned a value of 1, grade ++ is assigned a value of 2, and grade +++ is assigned a value of 3. Meanwhile, quantitative detection of WBC and bacteria was carried out with a urinary sediment analyser (UF-500i, SYSMEX).

Microbiologic analyses

The blood agar (BA, Thermo Fisher Scientific OXOID) and eosin-methylene blue (EMB, Thermo Fisher Sci-

entific OXOID) were used as the medium for urine culture. Each urine specimen (0.01 ml) was separately inoculated onto BA and EMB medium using a 0.01 ml calibrated loop, and then incubated aerobically at 37°C for 48 hours. The agar plates with one or two possible urinary pathogens at a concentration of $\geq 10^5$ colony forming unit/ml (cfu/ml) were considered as positive cultures,⁵ additionally, the agar plates with three or more pathogens were regarded as contaminated and excluded from study. According to urine culture results, the enrolled subjects were divided into the culture positive and sterile groups. The microorganisms were identified by VITEK System (bioMérieux, France), and the culture positive group was further divided into the Gram positive and negative subgroups according to the identified results.

Measurement of MPO concentration

MPO concentration in urine was determined with immunoturbidimetric method (Beijing Strong Biotechnologies, BSBE) with an OLYMPUS AU-2700 analyser (Japan), the result was reported as nanograms of MPO per milliliter of urine. To avoid the impact of urine volume on MPO concentration, MPO values were normalized to urinary creatinine concentration.⁵ Urinary creatinine level was measured by creatinine enzyme method (Merit Choice Bioengineering) with OLYMPUS AU-2700, the result was expressed as $\mu\text{mol/L}$. Ratio of MPO to creatinine (MCR) was ultimately reported as ng/g.

Statistical analysis

Statistical analysis was performed by SPSS (Version 16.0), Medcalc (15.2.2) and GraphPad Prism 5 (Version 5.01). Continuous data underwent normality test using skewness-kurtosis method. Firstly, if continuous data were normally distributed, *t* test was carried out for group comparison. Secondly, if continuous data were not normally distributed, group comparison was therefore performed using *t* test on log-transformed values that conformed to normal distribution. Thirdly, if the data did not follow a lognormal distribution, group comparison was performed using *nonparametric* test.

Levels of laboratory indicators in urine obtained from the urinary culture positive group and the sterile group were compared using Receiver operating characteristics (ROC); the comparisons were also performed between the gram positive and the negative subgroups. Difference in area under the curve (AUC) of laboratory parameters between the urine culture posi-

tive group and the negative group was compared with Medcalc software.

Correlation of MCR with uncontinuous data was analyzed by using *Spearman* correlation analysis, while correlation of MCR with continuous data was analyzed with *Pearson* correlation analysis. The sensitivity, specificity, positive predict value, negative predict value and accuracy of the above indicators for diagnosis of UTI were analyzed.

Two sided *P* values <0.05 were considered statistically significant.

RESULTS

Results of patients enrollment

According to the results of urine culture, 157 urine culture positive and 96 sterile subjects were included in present study (Fig. 1).

Results of urine cultures

Through the urine cultures, 165 bacteria were isolated from 157 urine culture positive specimens, 1 strain bacterium was identified in 149 samples and 2 bacteria were identified in 8 positive cultures. For the 157 positive sample, 36 were gram positive and 121 were negative. Distribution of bacteria in the 157 culture positive specimens is shown in Table 1.

Demographic features and laboratory indicators

Statistical analysis showed all the continuous data except for ages presented non-normal distribution. After logarithmic transformation in 2 as the base, all transformed data showed a normal distribution, so the MCR, WBC count, and bacteria were separately presented as $\log_2^{\text{MCR}}$, $\log_2^{\text{WBC}}$ (quantitative), and $\log_2^{\text{bacteria}}$.

The sex ratio between the urinary culture positive group and the sterile group was not statistically significant ($\chi^2=1.165$, $P=0.204$). The median age (years) of the urinary culture positive group was significantly higher than that of the sterile group ($Z=-3.583$, $P=0.001$). The values of $\log_2^{\text{MCR}}$ ($t=-12.453$, $P=0.001$), $\log_2^{\text{WBC}}$ (quantitative) ($t=-10.332$, $P=0.001$), $\log_2^{\text{bacteria}}$ ($t=-9.297$, $P=0.001$) and WBC (semi-quantitative) ($Z=-7.580$, $P=0.001$) between the two groups had significant difference. (Table 2)

Differences in AUC of $\log_2^{\text{MCR}}$, $\log_2^{\text{WBC}}$ (quantitative), $\log_2^{\text{bacteria}}$ and WBC (semi-quantitative) between the urine culture positive and sterile groups were 0.854, 0.818, 0.796 and 0.774, respectively, and optimum

Figure 1. A schematic view of subject selection.

UTI: urinary tract infection; eGFR: estimated glomerular filtration rate; BA: blood agar; EMB: eosin-methylene blue.

Table 1. Distribution of bacteria in 157 culture positive specimens

Items	Number of positive case [n (%)]
Gram positive group (n=36)	
<i>E. faecalis</i>	7 (4.46)
<i>E. faecium</i>	15 (9.55)
<i>S. epidermidis</i>	4 (2.55)
<i>S. aureus</i>	5 (3.18)
<i>S. haemolyticus</i>	2 (1.27)
<i>S. hemolytic</i>	2 (1.27)
<i>E. casseliflavus</i>	1 (0.64)
Gram negative group (n=121)	
<i>E. coli</i>	86 (54.78)
<i>P. mirabilis</i>	3 (1.91)
<i>K. pneumoniae</i>	20 (12.74)
<i>M. morgani</i>	1 (0.64)
<i>C. koseri</i>	1 (0.64)
<i>P. aeruginosa</i>	1 (0.64)
<i>S. marcescens</i>	1 (0.64)
<i>E. coli</i> + <i>K. pneumoniae</i>	1 (0.64)
<i>E. coli</i> + <i>S. marcescens</i>	2 (1.27)
<i>P. mirabilis</i> + <i>S. marcescens</i>	1 (0.64)
<i>P. mirabilis</i> + <i>K. pneumoniae</i>	1 (0.64)
<i>P. aeruginosa</i> + <i>P. mirabilis</i>	1 (0.64)
<i>E. coli</i> + <i>P. mirabilis</i>	2 (1.27)

cutoff values were 7.6 ng/g, 6.1/μl, 11.3/μl and 1, respectively (Table 3 and Fig. 2). The corresponding cutoff values for MCR, WBC (quantitative) and bacteria were 194.0 ng/g, 68.6/μl and 2521.4/μl, respectively.

The AUC differences between $\log_2^{\text{MCR}}$ and $\log_2^{\text{WBC}}$ (quantitative), $\log_2^{\text{MCR}}$ and $\log_2^{\text{bacteria}}$, $\log_2^{\text{MCR}}$ and WBC (semi-quantitative) were 0.0354 ($Z=1.309$, $P=0.191$), 0.0576 ($Z=1.670$, $P=0.095$) and 0.0797 ($Z=2.638$, $P=0.008$), respectively (Table 4).

Among of the urine culture positive group, $\log_2^{\text{MCR}}$ level of the gram positive subgroups was significantly lower than that of the gram negative subgroups (7.2 ± 2.5 vs. 9.0 ± 2.4 , $t=4.016$, $P=0.001$). However, there was no significant difference in $\log_2^{\text{MCR}}$ between patients infected with two bacteria ($n=8$, 9.5 ± 2.7) and ones detected to have one bacterial isolate ($n=149$, 8.5 ± 2.5 ; $t=-1.018$, $P=0.310$).

The correlation between $\log_2^{\text{MCR}}$ and $\log_2^{\text{WBC}}$ (quantitative), $\log_2^{\text{bacteria}}$, WBC (semi-quantitative) were 0.708 (Pearson correlation, $P=0.001$), 0.381 (Pearson, $P=0.001$) and 0.606 (Spearman correlation, $P=0.001$), respectively.

Table 2. Comparisons of demographic features and laboratory indicators between the urine culture positive and sterile groups[§]

Groups	n	Gender (M/F)	Age* (yrs)	log ₂ ^{MCR}	log ₂ ^{WBC} (quantitative)	log ₂ ^{bacteria}	WBC# (semi-quantitative)
Sterile group	96	20/76	62 (45, 75)	5.4±1.5	5.2±1.8	8.2±2.8	1 (0.5, 1)
Culture positive group	157	23/134	52 (39, 64)	8.6±2.5	8.0±2.5	11.4±2.5	2 (1, 3)
P value		0.204	0.001	0.001	0.001	0.001	0.001

§: Plus-minus values are means±SD. #Data were expressed as median and interquartile range.

M: male; F: female; MCR: myeloperoxidase to creatinine ratio; WBC: white blood cell.

Table 3. The capability of laboratory indicators to differentiate the urine culture positive group from the sterile group

Items	AUC	SE	95% CI	Cutoff value	SEN (%)	SPE (%)	PPV (%)	NPV (%)	Accuracy (%)
log ₂ ^{MCR}	0.854	0.0238	0.807-0.900	7.6 ng/g	66	95	95	63	80
log ₂ ^{WBC} (quantitative)	0.818	0.0262	0.767-0.869	6.1 /μl	76	77	84	66	76
log ₂ ^{bacteria}	0.796	0.0278	0.741-0.851	11.3 /μl	55	92	89	54	73
WBC (semi-quantitative)	0.774	0.0281	0.719-0.829	1	63	77	82	56	70

AUC: area under the curve; SE: standard error; CI: confidence interval; SEN: sensitivity; SPE: specificity; PPV: positive predictive value; NPV: negative predictive value.

Figure 2. Analysis of ability of four biomarkers to differentiate the urine culture positive group from the sterile group using receiver operating characteristic curve.

DISCUSSION

UTI affects a wide range of people. The present laboratory tests such as routine urine test and urine culture all have their own shortcomings, therefore, we

need some markers with high sensitivity and specificity for diagnosis of UTI. There are several results of the present study. First of all, MCR level of the urine culture positive group was significantly higher than that of the sterile group. Secondly, through analysis of four above indicators, the ability of MCR in differentiating the urine culture positive group from the sterile group was significantly higher than that of WBC (semi-quantitative), nevertheless, no statistical difference was observed between MCR and WBC (quantitative) or bacteria. Thirdly, MCR level of the gram negative group was significantly higher than that of the gram positive group. Finally, MCR was statistically correlated with other urinary indicators, especially of WBC.

MPO is an important member of the haem peroxidase-cyclooxygenase superfamily. This enzyme is physiologically expressed in circulating neutrophils, monocytes and some tissue macrophages including microglia.^{8, 19} MPO, the most abundant neutrophil granule protein, plays a key role in various functions of neutrophils in innate and adaptive immunity.²⁰⁻²¹ MPO is synthesized during myeloid differentiation that constitutes the major component of the neutrophil azurophilic granules.²² Upon phagocyte activation in pe-

Table 4. AUC difference between log₂^{MCR} and other indicators

Items	AUC difference	SE	95% CI	Z	P value
log ₂ ^{WBC} (quantitative)	0.0354	0.0270	-0.0176-0.0884	1.309	0.191
log ₂ ^{bacteria}	0.0576	0.0345	-0.0100-0.1250	1.670	0.095
WBC (semi-quantitative)	0.0797	0.0302	0.0205-0.1390	2.638	0.008

ripheral blood, tissues, or fluids, MPO is released from leukocytes into both the phagolysosomal compartment and the extracellular milieu.²³ The role of MPO in the inflammatory reactions is well studied, which contributes to killing the pathogens, but it is also implicated in several inflammatory syndromes such as Parkinson's disease,²⁴ atherosclerosis,²⁵ chronic kidney disease,²⁶⁻²⁷ leukemia,²⁸ diabetes mellitus,²⁹ and Alzheimer's disease³⁰ and so on.

The present study found that urinary MCR level was significantly higher in the urinary culture positive group than that of the sterile group, and the result is consistent with previous study,⁵ which suggests that MCR may be used as a useful marker for diagnosis of UTI. However, the accuracy of urinary MCR for UTI diagnosis of the present study seems inferior to the former study. This may be due to different measurement methods applied to analyze MPO, in the current study the amount of MPO to be measured, whereas in the previous study the enzyme activity of MPO to be determined. Besides MCR, urinary WBC and bacteria were also measured in the present study, afterwards, we compared the capacity of MCR, WBC and bacteria in differentiating the urine culture positive group from the sterile group. The result showed that MCR was superior to WBC (semi-quantitative). Although AUC of MCR seems superior to bacteria and WBC (quantitative), it does not reach a statistical significance. Based on the above research results, we conclude that urinary MCR could be used as a new biomarker for the diagnosis of UTI, which even seems superior to some indicators of urinary routine test.

Escherichia coli is the most predominant pathogen causing 80%-90% of community-acquired UTI and 30%-50% of nosocomially-acquired UTI.¹ In clinical practice, a urinary bacterial culture, biochemical identification and susceptibility test takes approximately 2 days. Consequently, physicians usually prescribe antibiotics against gram negative bacteria for empirical therapy before a drug susceptibility test is acquired. However, there are still a small part of UTI patients who are infected by gram positive bacteria rather than gram negative ones, accordingly, it is very important to preliminarily determine the type of bacteria before empiric medication. The present research revealed that MCR level of the gram negative group was higher than that of the gram positive group, we conclude that MCR could be served as a marker for preliminary inference on the types of infectious micro-

organisms, which can afford more accurate guidance for physicians to prescribe antibiotics for UTI patients.

The present study revealed that MCR level was statistically correlated with WBC and bacteria, especially WBC. In clinical practice, low urinary osmolality or too long urinary retention time usually account for WBC destruction. Combined with the above experimental results, we infer that MCR might be preferable to reflecting urinary WBC counts in some special conditions.

There are several limitations of the present study. First, the proportion of contaminated specimens was a bit high (49/302); secondly, we did not detect the MCR level in patients with contaminated specimens; finally, when calculating the sensitivity and specificity of MCR in diagnosis of UTI, the sample size was still small.

In conclusion, MCR is positively correlated with WBC counts in urinary, which can be served as a promising biomarker for diagnosis of UTI. In addition, MCR could be even used to infer infectious bacteria types of UTI.

Conflicts of interest statement

The authors declare that they have no competing interests.

REFERENCES

1. Ejrnaes K. Bacterial characteristics of importance for recurrent urinary tract infections caused by *Escherichia coli*. Dan Med Bull 2011; 58(4):B4187.
2. American College of Obstetricians and Gynecologists. ACOG Practice Bulletin No. 91: treatment of urinary tract infections in nonpregnant women. Obstet Gynecol 2008; 111(3):785-94. doi: 10.1097/AOG.0b013e-318169f6ef.
3. Dune TJ, Price TK, Hilt EE, et al. Urinary symptoms and their associations with urinary tract infections in urogynecologic patients. Obstet Gynecol 2017; 130(4):718-25. doi: 10.1097/AOG.0000000000002239.
4. Gupta K, Grigoryan L, Trautner B. Urinary tract infection. Ann Intern Med 2017; 167(7):ITC49-ITC64. doi: 10.7326/AITC201710030.
5. Ciragil P, Kurutas EB, Miraloglu M. New markers: urine xanthine oxidase and myeloperoxidase in the early detection of urinary tract infection. Dis Markers 2014; 2014:269362. doi: 10.1155/2014/269362.
6. Kalinderi K, Delkos D, Kalinderis M, et al. Urinary tract infection during pregnancy: current concepts on a

- common multifaceted problem. *J Obstet Gynecol* 2018; 38(4):1-6. doi: 10.1080/01443615.2017.1370579.
7. Bardsley A. Diagnosis, prevention and treatment of urinary tract infections in older people. *Nurs Older People* 2017; 29(2):32-8. doi: 10.7748/nop.2017.e884.
8. Chu CM, Lowder JL. Diagnosis and treatment of urinary tract infections across age groups. *Am J Obstet Gynecol* 2018; 219(1):40-51. doi: 10.1016/j.ajog.2017.12.231.
9. Demilie T, Beyene G, Melaku S, et al. Diagnostic accuracy of rapid urine dipstick test to predict urinary tract infection among pregnant women in Felege Hiwot Referral Hospital, Bahir Dar, North West Ethiopia. *BMC Res Notes* 2014; 7:481. doi: 10.1186/1756-0500-7-481.
10. Masinde A, Gumodoka B, Kilonzo A, et al. Prevalence of urinary tract infection among pregnant women at Bugando Medical Centre, Mwanza, Tanzania. *Tanzan J Health Res* 2009; 11(3):154-9.
11. Kocer D, Sariguzel FM, Ciraci MZ, et al. Diagnostic accuracy of a new urinalysis system, DongJiu, for diagnosis of urinary tract infection. *Ann Clin Lab Sci* 2015; 45(6):686-91.
12. Nasioudis D, Witkin SS. Neutrophil gelatinase-associated lipocalin and innate immune responses to bacterial infections. *Med Microbiol Immunol* 2015; 204(4):471-9. doi: 10.1007/s00430-015-0394-1.
13. Forster CS, Johnson K, Patel V, et al. Urinary NGAL deficiency in recurrent urinary tract infections. *Pediatr Nephrol* 2017; 32(6):1077-80. doi: 10.1007/s00467-017-3607-6.
14. Price JR, Guran L, Lim JY, et al. Neutrophil gelatinase-associated lipocalin biomarker and urinary tract infections: a diagnostic case-control study (NUTI Study). *Female Pelvic Med Reconstr Surg* 2017; 23(2):101-7. doi: 10.1097/SPV.0000000000000366.
15. Kim BH, Yu N, Kim HR, et al. Evaluation of the optimal neutrophil gelatinase-associated lipocalin value as a screening biomarker for urinary tract infections in children. *Ann Lab Med* 2014; 34(5):354-9. doi: 10.3343/alm.2014.34.5.354.
16. Podrez EA, Abu-Soud HM, Hazen SL. Myeloperoxidase-generated oxidants and atherosclerosis. *Free Radic Biol Med* 2000; 28(12):1717-25.
17. Zederbauer M, Jantschko W, Neugschwandtner K, et al. Role of the covalent glutamic acid 242-heme linkage in the formation and reactivity of redox intermediates of human myeloperoxidase. *Biochemistry* 2005; 44(17):6482-91. doi: 10.1021/bio501737.
18. Levey AS, Inker LA and Coresh J. GFR estimation: from physiology to public health. *Am J Kidney Dis* 2014; 63(5):820-34. doi: 10.1053/j.ajkd.2013.12.006.
19. Lazarevic-Pasti T, Leskovic A, Vasic V. Myeloperoxidase inhibitors as potential drugs. *Curr Drug Metab* 2015; 16(3):168-90.
20. Odobasic D, Kitching AR, Holdsworth SR. Neutrophil-mediated regulation of innate and adaptive immunity: the role of myeloperoxidase. *J Immunol Res* 2016; 2016:2349817. doi: 10.1155/2016/2349817.
21. Klebanoff SJ. Myeloperoxidase. *Proc Assoc Am Physicians* 1999; 111(5):383-9.
22. Unubol M, Yavasolu I, Kacar F, et al. Relationship between glycemic control and histochemical myeloperoxidase activity in neutrophils in patients with type 2 diabetes. 2015; 7(1):119. doi: 10.1186/s13098-015-0115-3.
23. Pattison DI, Davies MJ, Hawkins CL. Reactions and reactivity of myeloperoxidase-derived oxidants: differential biological effects of hypochlorous and hypothiocyanous acids. *Free Radic Res* 2012; 46(8):975-95. doi: 10.3109/10715762.2012.667566.
24. Ortiz GG, Morales-Sanchez EW, Pacheco-Moises FP, et al. Effect of melatonin administration on cyclooxygenase-2 activity, serum levels of nitric oxide metabolites, lipoperoxides and glutathione peroxidase activity in patients with Parkinson's disease. *Gac Med Mex* 2017; 153(Supl. 2):S72-S81. doi: 10.24875/GMM.M000008.
25. Long L, Song Y. Myeloperoxidase: a promising therapeutic target in prevention of atherosclerosis. *Int J Cardiol* 2018; 256:15. doi: 10.1016/j.ijcard.2017.10.057.
26. Soubhye J, Aldib I, Delporte C, et al. Myeloperoxidase as a target for the treatment of inflammatory syndromes: mechanisms and structure activity relationships of inhibitors. *Curr Med Chem* 2016; 23(35):3975-4008.
27. Kusic B, Miric D, Dragojevic I, et al. Role of myeloperoxidase in patients with chronic kidney disease. *Oxid Med Cell Longev* 2016; 2016:1069743. doi: 10.1155/2016/1069743.
28. Rossetto Burgos RC, Ramautar R, Van Wijk EPA, et al. Pharmacological targeting of ROS reaction network in myeloid leukemia cells monitored by ultra-weak photon emission. *Oncotarget* 2018; 9(2):2028-34. doi: 10.18632/oncotarget.23175.
29. Wiedenmann T, Dietrich N, Fleming T, et al. Modulation of glutathione peroxidase activity by age-de-

pendent carbonylation in glomeruli of diabetic mice. J Diabetes Complications 2018; 32(2):130-8. doi: 10.1016/j.jdiacomp.2017.11.007.

30. Ji W, Zhang Y. The association of MPO gene pro-

motor polymorphisms with Alzheimer's disease risk in Chinese Han population. Oncotarget 2017; 8(64):107870-6. doi: 10.18632/oncotarget.22330.

尿液髓过氧化物酶肌酐比值作为诊断泌尿系感染的新标志物

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关键词: 尿液; 髓过氧化物酶; 诊断; 泌尿系感染

目的 探讨尿液髓过氧化物酶与肌酐比值(MCR)是否可作为泌尿系感染(UTI)诊断的指标。

方法 将疑似UTI的患者根据尿培养结果分为培养阳性组和培养阴性组。并对两组患者尿液MCR、白细胞(WBC)和细菌进行检测和比较。

结果 253例患者中有157例尿培养阳性, 96例培养阴性。尿MCR、WBC和细菌分别以2为基数取对数。尿液培养阳性组和阴性组间log₂MCR、log₂WBC(定量)、log₂bacteria、WBC(半定量)水平分别为(8.6±2.5比5.4±1.5, t=-12.453, P=0.001)、(8.0±2.5比5.2±1.8, t=-10.332, P=0.001)、(11.4±2.5比8.2±2.8, t=-9.297, P=0.001)、[2(1, 3)比1(0.5, 1), Z=-7.580, P=0.001], 差异均有统计学意义。在尿培养阳性组中, 革兰阳性菌组与阴性菌组的log₂MCR水平分别为7.2±2.5和9.0±2.4, t=4.016, P=0.001, 差异有统计学意义。log₂MCR与log₂WBC(定量)、log₂bacteria、WBC(半定量)相关性(Pearson)分别为0.708(P=0.001)、0.381(P=0.001)、0.606(P=0.001)。

结论 MCR与WBC计数呈正相关, 可作为诊断UTI新的标志物。MCR甚至可以用于初步推断UTI的细菌类型。