lyzer (Dade-Behring). GFR was estimated with the Cockcroft-Gault formula (6). Statistical analysis of the data before and after treatment was performed with the paired t-test (P <0.05 considered significant).

In the patients with hyperthyroidism, after treatment mean (SD) serum creatinine decreased from 90 (22) μmol/L to 77 (18) μmol/L (P <0.0001); accordingly, estimated GFR increased (P <0.0001; Fig. 1A). On the other hand, cystatin C increased after treatment (Fig. 1B). In the patients with hyperthyroidism, serum creatinine increased from 50 (13) μmol/L to 72 (18) μmol/L (P <0.0001), and the estimated GFR decreased accordingly after treatment (Fig. 1A). Cystatin C, however, decreased significantly after treatment (Fig. 1B). Paradoxically, cystatin C decreased in hyperthyroidism, in contrast to the values for creatinine and GFR. The values for all three markers moved toward reference values for euthyroidism. This finding was consistent for both hypo- and hyperthyroid patients.

We offer the following possible explanations for our findings. In hyperthyroidism, creatinine increases; accordingly, the estimated GFR, which is based on creatinine, decreases. We could find only one study that calculated GFR by use of isotopes, i.e., the plasma clearance of CrEDTA, in patients with hyperthyroidism (3). That study demonstrated a diminished GFR in hyperthyroidism, which was reversible in the euthyroid state. Thyroid hormones have significant effects on renal hemodynamics, renal handling of salt and water, and the active tubular transport processes for Na⁺, K⁺, and H⁺ (7). It is possible that tubular creatinine secretion is diminished in hyperthyroidism, thereby increasing serum creatinine concentrations. We observed the opposite effect in the hyperthyroid patients. In addition, because the thyroid state influences metabolism in general, it may influence the production of cystatin C. This would lead to lower cystatin C concentrations in hyperthyroidism and higher concentrations in hyperthyroidism. In that case, the production rate of cystatin C may not be constant, as reported recently.

In summary, in patients with thyroid dysfunction, plasma creatinine concentrations could be influenced by effects of thyroid hormones on the renal tubular cells, and plasma cystatin C concentrations could be influenced by the effects of thyroid hormones on cystatin C production. On the basis of our data and the data presented in two very recently published reports (8, 9), we conclude that serum creatinine and estimated GFR by the Cockcroft-Gault formula remain better estimates of GFR than does cystatin C and that cystatin C cannot be used without knowledge of the thyroidal state. However, more investigation is needed because none of the studies used a “golden standard” for GFR determination.

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References


Jan G. den Hollander¹
Raymond W. Wulkan²
Mart J. Mantel²
Arie Berghout¹

Departments of ¹Internal Medicine and ²Clinical Chemistry
Medical Center Rotterdam Zuid
Location Zuid
3075 EA Rotterdam, The Netherlands

*Address correspondence to this author at: Department of Internal Medicine, Medical Center Rijnmond Zuid, Location Zuid, Groene Hilledijk 315, 3075 EA Rotterdam, The Netherlands. Fax 31-10-2903361; e-mail BerghoutA@MCRZ.nl.

Microscopic Urinalysis and Automated Flow Cytometry in a Nephrology Laboratory

To the Editor:

In their recent report, Ottiger and Huber (1) compared the UF-100 flow cytometer and the KOVA system and suggested an algorithm for the selection of samples for microscopic analysis. They found that urine samples from nephrology patients had higher microscopic review rates. We agree with them that automated systems foster rapid and standardized analysis of formed elements and offer significant labor savings (2–4), but we think that such a study may lead to different results in a laboratory of nephrology, where the prevalence of renal diseases and pathologic findings is higher.

We collected 298 consecutive midstream urine samples from patients with known or suspected renal diseases. The samples were first examined with a Sysmex UF-50 (software version 0.5; TOA Medical Electronics) and then with a phase-contrast microscope (5), according to the European guidelines, at low (×100) and high (×400) magnification, by the same team (one biologist and one nephrologist, who independently analyzed the samples and then compared and discussed the results). The upper reference limits for phase-contrast microscopy used in our laboratory are as follows: erythrocytes, <2/high-power field (HPF); leuko-
Concordant results, % 83.9 88.6 53.1 92.2
Flow cytometry (UF-50), n (%) 115 (39%) 88 (30%) 55 (18%) 9 (3%)
Microscopy, n (%) 131 (44%) 84 (28%) 153 (51%) 16 (5%)

We also tried to evaluate whether flow cytometry is useful in the analysis of erythrocyte dysmorphism by applying the Kitasato criteria (6, 7). However, this system relies on erythrocyte volume and size, and the flow cytometer distinguishes erythrocytes on the basis of cellular diameter but cannot recognize dysmorphic erythrocytes with altered shape, such as acanthocytes or codocytes (8). Thus, in our study we observed that of 131 samples with microhematuria by microscopy, 41 (31%) had predominantly dysmorphic erythrocytes according to both methods, whereas 59 (45%) had predominantly normal erythrocytes, but 16 (12%) revealed their dysmorphism only when analyzed by phase-contrast microscopy with a significant presence of altered cell shape (acanthocytes), and 15 (11%) showed their dysmorphism only when analyzed by flow cytometry, probably because of the presence of high amounts of yeasts or erythrocytes with different sizes.

In conclusion, combining the automated and traditional analyses of urinary formed elements in general laboratories—starting with automated cell counting followed by microscopic analysis, which is more specific in revealing morphologic aspects—may be a time-saving policy. In a laboratory of nephrology, however, where samples have a strong preselection, such an algorithm is not applicable and all samples must be analyzed by phase-contrast microscopy. Nonetheless, the use of the automated procedure may help to save time on red and white cell counts, thus allowing the operators to dedicate more time to the morphologic definitions.

We suggest to the authors to use microscopic review of all samples referred from selected settings with a high prevalence of renal diseases, as those samples may be pathologic even in the absence of review flags from the flow cytometer.

We give special thanks to Dasit s.p.a. Italy, which provided us with a SYSMEX UF-50 (Toa Medical Electronics), technical assistance, reagents, and disposable equipment in support of our study.

References

Massimo Gai*
Giorgina B. Piccoli
Giuseppe P. Segoloni
Giacomo Lanfranco
Laboratory of Nephrology
University of Torino
10126 Turin, Italy

*Address correspondence to this author at: Azienda Ospedaliera “San Giovanni Battista” di Torino, U.O.A.D.U. Nefrologia, Dialisi e Trapianto, Corso Bramante 88, 10126 Torino, Italy. Fax 39-0116963158; e-mail massimogai@katamail.com.

Stability of N-Terminal Pro-Brain Natriuretic Peptide after Storage

To the Editor:

Cardiac natriuretic peptides are of interest for their potential role in

Table 1. Pathologic samples for erythrocytes, leukocytes, casts, and crystals and concordance of methods after analysis of 298 urine samples by microscopy and flow cytometry.

<table>
<thead>
<tr>
<th></th>
<th>RBCs, ≥ 2 cells/HPF</th>
<th>WBCs, &gt;4 cells/HPF</th>
<th>Pathologic casts</th>
<th>Significant crystalluria</th>
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<tbody>
<tr>
<td>Microscopy, n (%)</td>
<td>131 (44%)</td>
<td>84 (28%)</td>
<td>153 (51%)</td>
<td>16 (5%)</td>
</tr>
<tr>
<td>Flow cytometry (UF-50), n (%)</td>
<td>115 (39%)</td>
<td>88 (30%)</td>
<td>55 (18%)</td>
<td>9 (3%)</td>
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<tr>
<td>Concordant results, %</td>
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<td>88.6</td>
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<td>K (Cohen)</td>
<td>0.67</td>
<td>0.72</td>
<td>0.08</td>
<td>0.043</td>
</tr>
</tbody>
</table>

* RBC, red blood cell (erythrocyte); WBC, white blood cell (leukocyte).