β-Trace Protein, Cystatin C, β₂-Microglobulin, and Creatinine Compared for Detecting Impaired Glomerular Filtration Rates in Children

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Background: Because of the limitations of serum creatinine as a marker of glomerular filtration rate (GFR) in children, we assessed the diagnostic accuracy of the novel marker β-trace protein (BTP) in comparison with cystatin C (Cys-C), β₂-microglobulin (β₂-MG), and creatinine as conventional indicators of reduced GFR.

Methods: We obtained serum samples from 225 children (age range, 0.2–18 years) with various renal pathologies who were referred for nuclear medicine clearance investigations (technetium–diethylenetriamine pentaacetic acid or chromium-EDTA). We measured Cys-C, BTP (nephelometric tests; Dade Behring), β₂-MG (Tinaquant; Roche), and creatinine (enzymatic assay; Creatinine-PAP; Roche).

Results: Seventy-five children had reduced GFR (<90 mL·min⁻¹·1.73 m⁻²). One hundred fifty children (independent of gender and age) with values >90 mL·min⁻¹·1.73 m⁻² comprised the control group with gaussian distributions of BTP and Cys-C concentrations. The upper reference limits (97.5 percentile) were 1.01 mg/L for BTP and 1.20 mg/L for Cys-C. The correlations of nuclear medicine clearance with the reciprocals of BTP, Cys-C, and the Schwartz GFR estimate were significantly higher (r = 0.653, 0.765, and 0.706, respectively; P <0.05) than with the reciprocal of creatinine or β₂-MG (r = 0.500 and 0.557, respectively). ROC analysis showed a significantly higher diagnostic accuracy of BTP, Cys-C, and the GFR estimate for the detection of impaired GFR than serum creatinine (P <0.05). Compared to creatinine, BTP increased the diagnostic sensitivity by ~30%, but it was not more sensitive than Cys-C or the Schwartz GFR estimate.

Conclusions: BTP is superior to serum creatinine and an alternative for Cys-C to detect mildly reduced GFR in children, but it is not better than the Schwartz GFR estimate.

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Although it is a crude marker, serum creatinine is the most widely used to predict glomerular filtration rate (GFR).9 Creatinine concentrations are insensitive to mild to moderate reductions in GFR. In childhood, the age and muscle mass dependency of serum creatinine complicates GFR assessment even when body length/creatinine ratios are used (1, 2). Low-molecular weight proteins have been suggested to replace serum creatinine. β₂-microglobulin (β₂-MG) has been advocated as a better predictor of GFR (3), but its serum concentration can increase as an acute-phase reactant in disorders, such as lupus nephritis, that clearly require adequate assessment of GFR. Serum or plasma cystatin C (Cys-C) may be better markers for GFR than serum creatinine [reviewed in Ref. (4)]. Cys-C offers an advantage over creatinine because of its age and gender independence (5, 6), but its diagnostic sensitivity for impaired GFR in pediatric patients, particularly in patients with only mildly impaired renal function, has not

*Nonstandard abbreviations: GFR, glomerular filtration rate; β₂-MG, β₂-microglobulin; Cys-C, cystatin C; BTP, β-trace protein; ⁵¹Cr-EDTA, chromium-EDTA; and ⁹⁹mTc-DTPA, technetium–diethylenetriamine pentaacetic acid.

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Received September 5, 2001; accepted January 24, 2002.
been better than that of the height/creatinine ratio (Schwartz formula) (7).

β-Trace protein (BTP) is a low-molecular weight glycoprotein with 168 amino acids and a molecular weight of 23 000–29 000, depending on the degree of glycosylation. BTP belongs to the lipocalin protein family; its biologic significance as prostaglandin D synthase is under investigation (8), and it is isolated primarily from cerebrospinal fluid (9). Serum BTP is increased in patients with renal diseases (8). It has been reported to be a better indicator of reduced GFR (estimated by inulin clearance) than serum creatinine in the creatinine-blind range (10), but not better than Cys-C (11). Further studies on this interesting new marker of GFR remain scarce (12), and to the best of our knowledge, there are no reports about the pediatric age range.

We used data from two university children centers to address the following goals: (a) to establish provisional reference limits of the new marker BTP in children; (b) to evaluate the relationship between BTP and other low-molecular weight proteins such as Cys-C and β2-MG to the GFR, using chromium-EDTA (51Cr-EDTA) or technetium–diethylenetriamine pentaacetic acid (99mTc-DTPA) clearance as the gold-standard comparison method; (c) to evaluate the diagnostic performance of BTP in comparison with the other low-molecular weight proteins to detect reduced GFR; and (d) to evaluate the usefulness of low-molecular weight proteins in serum in comparison with the conventional indicators, serum creatinine and the Schwartz GFR estimate.

This study compared serum analytes with the results for Cys-C, BTP, and 2-MG. Serum BTP was measured in only the German patients. Samples were analyzed without knowledge of GFR tests, which were performed first. Serum creatinine was measured with an enzymatic assay (Creatinine-PAP; Roche Diagnostics), and the factors 38 for children >1 year and 48 for adolescent males [Schwartz GFR estimate (17), with a 20% correction for enzymatic measurement of creatinine] were used to calculate the Schwartz GFR estimate (7). The formula reads as follows:

\[
\text{GFR estimate} = \frac{\text{height (cm)} \times \text{constant}}{\text{serum creatinine (μmol/L)}}
\]

Determination of Cys-C was performed with the N Latex Cystatin C reagent set (Dade Behring) on a Behring BN ProSpec analyzer. β2-MG was measured with the Tinaquant reagent set (Roche Diagnostics) on the Hitachi 717 analyzer (Roche Diagnostics). Interassay imprecisions (CVs) were 2.3% and 1.4% at 114 and 499 μmol/L, respectively, for creatinine (n = 31); 3.2% at 1.49 mg/L for Cys-C (n = 10); and 3.1% and 2.7% at 2.55 and 5.25 mg/L, respectively, for β2-MG (n = 10). BTP was measured with a newly developed nephelometric research assay (N Latex βTP) on a BN ProSpec analyzer (Dade Behring). The assay is based on the principle of latex particle-enhanced immunonephelometry using rabbit polyclonal antibodies against BTP. Calibration is performed with a seven-point reference curve prepared automatically from a single calibrator. Standardization of the assay is based on highly purified BTP from cerebrospinal fluid (Dade Behring). The identity and the grade of purification were monitored...
by sodium dodecyl sulfate–polyacrylamide gel electrophoresis for grade of purification and N-terminal amino acid sequencing for grade of purification and identity, compared with theoretical sequence. The BTP content was determined by quantitative amino acid analysis. For the default sample dilution of 1:100 (1 part BTP sample plus 99 parts buffer), the basic measuring range is ~0.25–15.8 mg/L. The total analytical imprecision (intraassay plus interassay; n = 40) of the assay, calculated from two control materials and three serum samples with concentrations of 1.51–7.89 mg/L, was 2.3–6.5%.

STATISTICAL ANALYSIS

Statistical analysis was performed with the GraphPad Prism for Windows (Ver. 3.02; GraphPad Software) or SPSS for Windows (Ver. 10; SPSS Inc). The reference cohort with GFR values >90 mL \cdot min^{-1} \cdot 1.73 m^{-2} was subdivided into female and male age groups. Differences between the groups were tested with the Kruskal–Wallis nonparametric ANOVA and Mann–Whitney U-test. To compare the differences of the relative changes of the analytes from their upper reference limits in the various GFR ranges, the t-test of paired data was used. Associations between variables (e.g., age, creatinine, GFR) were assessed with the correlation coefficient according to Pearson (r). The central 95% reference intervals for Cys-C and BTP were calculated according to the IFCC recommendations (18). P < 0.05 was considered statistically significant. The diagnostic validity of Cys-C, BTP, \(\beta_2\)-MG, creatinine, and the height/creatinine ratio (Schwartz formula) (7, 17) to detect reduced GFR in comparison to the \(^{51}\)Cr-EDTA or \(^{99m}\)Tc-DTPA clearance was evaluated by ROC analysis (19). MedCalc for Windows (Ver. 6.11.001; MedCalc) was used for calculations of the area under the curve and the sensitivity/specificity data at certain cutoffs.

Results

REFERENCE INTERVALS OF BTP AND CYSC

We deliberately combined the data of the two centers because we believed that the evaluation should have included a large number of patients. We indeed applied two different, well-established, and comparable isotope methods for GFR determination (15, 16). Because there was no statistically significant difference between the Berlin and Ottawa patient cohorts with regard to age (Student t-test, P = 0.30), gender distribution (\(\chi^2\) test, P = 0.13), or GFR (Student t-test, P = 0.15), the two cohorts could be combined for a common evaluation of data. To confirm the agreement of both GFR methods used in this study, we compared the concentrations of creatinine, BTP, and Cys-C in GFR subgroups with nondifferent GFR values in both centers (50–70, 70–90, 90–110, and 110–130 mL \cdot min^{-1} \cdot 1.73 m^{-2}). The concentrations of the analytes in the particular subgroups were not different between the two study sites (P > 0.05). Most importantly, the same assays with comparable interassay imprecisions were used for the other GFR markers in both centers. The scatter plots of the three analytes BTP, Cys-C, and creatinine (Fig. 1) show an overlap of their concentrations measured in the two centers. The y-intercepts of the regression lines calculated for each analyte did not significantly differ (P > 0.05) between the two centers.

Because it is impossible to measure nuclear isotope clearances in children without suspicious pathology, we defined children with nonpathologic GFR values (>90 mL \cdot min^{-1} \cdot 1.73 m^{-2}) as the control group. Seventy-five patients had GFR values <90 mL \cdot min^{-1} \cdot 1.73 m^{-2}, defined as reduced GFR, and 150 patients had GFR values >90 mL \cdot min^{-1} \cdot 1.73 m^{-2} (Table 1). In the control group, all analytes had gaussian distributions (Kolmogorov–Smirnov test, P > 0.05). The concentrations of BTP, Cys-C, \(\beta_2\)-MG, and creatinine were independent of gender for the entire control group and for the subgroups of 1–6, 6–12,
and 12–18 years (P values between 0.059 and 0.975). Unlike serum creatinine (Fig. 1C), BTP (Fig. 1A) and the other two proteins, Cys-C (Fig. 1B) and β2-MG (data not shown), were not age dependent and showed slopes of the regression lines to the age for both genders that were not significantly different from zero (P values between 0.09 and 0.99). As shown for Cys-C and β2-MG, there was no statistically significant correlation between the BTP concentrations and age [r = −0.126 for males (P = 0.250); r = −0.216 for females (P = 0.087)]. The mean Cys-C concentrations for the different age ranges were as follows: 0.80 ± 0.19 mg/L (1–6 years); 0.84 ± 0.14 mg/L (6–12 years); and 0.82 ± 0.16 mg/L (12–18 years). The mean BTP concentrations for the different age ranges were as follows: 0.71 ± 0.19 mg/L (1–6 years); 0.68 ± 0.13 mg/L (6–12 years); and 0.65 ± 0.15 mg/L (12–18 years). These differences did not reach statistical significance (P > 0.05). Thus, as we had shown previously for Cys-C (5), age- and gender-independent reference values for BTP can be considered. We calculated the upper reference limits as mean +1.96 SD. The 97.5 percentiles and their 90% confidence intervals for BTP and Cys-C are given in Table 1. The corresponding values for creatinine, β2-MG, and the Schwartz GFR estimates have been included for comparison.

CONCENTRATIONS OF BTP, CYS-C, AND β2-MG AND THEIR RELATION TO GFR AND SERUM CREATININE
Mean nuclear medicine GFR in the whole group was 105 ± 37 mL·min⁻¹·1.73 m²⁻² (range, 7–235 mL·min⁻¹·1.73 m²⁻²). BTP behaved similarly to serum creatinine and Cys-C when plotted against nuclear medicine clearance. It was possible to draw nonlinear regression lines (exponential decays) between the concentrations of the three analytes and GFR or linear regression lines between their reciprocals and GFR (Fig. 1). The correlations between the nuclear medicine GFR clearance and the reciprocals were significantly higher (P < 0.05) for BTP (r = 0.653; Fig. 2A) and Cys-C (r = 0.765; Fig. 2B) [although not for β2-MG (r = 0.557; not shown in Fig. 2)] than for serum creatinine (r = 0.500; Fig. 2C). The correlation coefficient of the Schwartz GFR estimate (r = 0.706) was similar to the correlation coefficients of Cys-C and BTP.

DIAGNOSTIC PERFORMANCE
To evaluate the ability of BTP to detect reduced GFR, ROC analysis was performed on data from 150 children with a GFR >90 mL·min⁻¹·1.73 m²⁻² and 75 children with a GFR <90 mL·min⁻¹·1.73 m²⁻². The mean (SD) GFRs in the groups with GFRs above and below >90 mL·min⁻¹·1.73 m²⁻² were 105 (25) and 65 (20) mL·min⁻¹·1.73 m²⁻², respectively.

ROC plot results are summarized in Table 2. The areas under the ROC curves for BTP (0.912), Cys-C (0.943), β2-MG (0.899), and Schwartz GFR estimate (0.917) were not statistically different (P > 0.05), although there was a tendency toward the best area for Cys-C. The area under the curve for creatinine (0.840) was significantly smaller than that for Cys-C (difference between areas, 0.103; SE, 0.031; P < 0.001), BTP (difference between areas, 0.072; SE, 0.034; P = 0.036), and the Schwartz GFR estimate (difference between areas, 0.080; SE, 0.021; P = 0.001).

The clinical sensitivities and specificities were calculated at selected decision points of the ROC curves (Table 2). At the upper reference limits (97.5 percentiles), both BTP and Cys-C revealed higher sensitivities than creatinine, β2-MG, and the GFR estimate (61% vs 29%, 38%, and 31%, respectively) for reduced GFR. At the cutoff with a diagnostic specificity of 95%, BTP (68%) and Cys-C (80%) had higher sensitivities than did serum creatinine (35%) and β2-MG (32%), but not higher than that of Schwartz GFR estimate (68%; Table 2). At the cutoff with a diagnostic sensitivity of 95%, BTP, Cys-C, and the Schwartz GFR estimate did not differ regarding specificities as the overlapping confidence intervals show (Table 2). Cys-C

### Table 1. BTP, Cys-C, β2-MG, creatinine, and the Schwartz GFR estimate in children with GFR values of >90–150 and <90 mL·min⁻¹·1.73 m²⁻².

<table>
<thead>
<tr>
<th>GFR &gt;90 mL·min⁻¹·1.73 m²⁻²</th>
<th>Cutoff limits of the 95% reference interval†</th>
<th>Number of children</th>
<th>Median (range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BTP, mg/L</td>
<td>0.01 (0.97–1.05)</td>
<td>150</td>
<td>1.01 (0.60–4.87)</td>
</tr>
<tr>
<td>Cys-C, mg/L</td>
<td>1.20 (1.16–1.24)</td>
<td>150</td>
<td>1.35 (0.65–7.44)</td>
</tr>
<tr>
<td>β2-MG, mg/L</td>
<td>3.09 (2.88–3.30)</td>
<td>80</td>
<td>2.80 (1.59–7.62)</td>
</tr>
<tr>
<td>Creatinine, μmol/L</td>
<td>85.9 (81.8–89.9)</td>
<td>150</td>
<td>76.0 (14.1–530)</td>
</tr>
<tr>
<td>Schwartz GFR estimate, mL·min⁻¹·1.73 m²⁻²</td>
<td>56 (50.3–61.7)</td>
<td>150</td>
<td>65.0 (11.6–234)</td>
</tr>
</tbody>
</table>

† Data from children with nonpathologic GFR were gaussian and are presented as mean ± SD and the range of values (in parentheses). Children with impaired GFR had log-normally distributed data. Hence data are expressed as medians and range of values in parentheses.
(63%) and the GFR estimate (65%), but not BTP (52%) showed a higher specificity than creatinine (47%). Between BTP and Cys-C, no statistical differences ($P > 0.05$) in the specificity and sensitivity were found at the selected 95% sensitivity or specificity, respectively, and at the 97.5 percentiles. In addition, with expressions of the BTP, Cys-C, and creatinine concentrations as proportions of their upper reference limits, BTP and Cys-C showed a significantly ($P < 0.05$) greater proportional increase than creatinine at the different degrees of renal failure (Fig. 3). These results clearly demonstrate that BTP is a more sensitive marker than creatinine and shows diagnostic accuracy similar to that of Cys-C, but the Schwartz GFR estimate was equivalent to that of BTP and Cys-C.

### Table 2. Diagnostic accuracy (areas under the ROC curves, sensitivity, and specificity) of BTP, Cys-C, $\beta_2$-MG, creatinine, and the Schwartz GFR estimate to detect reduced GFR (<90 mL · min$^{-1}$ · 1.73 m$^{-2}$) in children.$^a$

<table>
<thead>
<tr>
<th>Analysis</th>
<th>Area under the ROC curve, mean ± SE</th>
<th>Sensitivity, %</th>
<th>Specificity, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>BTP, mg/L</td>
<td>0.912 ± 0.024</td>
<td>61 (51–71)</td>
<td>97 (94–99)</td>
</tr>
<tr>
<td>1.01$^b$</td>
<td>68 (58–77)</td>
<td>95 (88–98)</td>
<td>52 (45–59)</td>
</tr>
<tr>
<td>0.68$^c$</td>
<td>80 (69–88)</td>
<td>95 (91–98)</td>
<td></td>
</tr>
<tr>
<td>0.94$^d$</td>
<td>61 (50–72)</td>
<td>98 (94–100)</td>
<td></td>
</tr>
<tr>
<td>Cys-C, mg/L</td>
<td>0.943 ± 0.019</td>
<td>95 (87–99)</td>
<td>63 (55–71)</td>
</tr>
<tr>
<td>1.20$^b$</td>
<td>38 (25–54)</td>
<td>94 (86–98)</td>
<td></td>
</tr>
<tr>
<td>0.87$^c$</td>
<td>95 (85–99)</td>
<td>54 (44–63)</td>
<td></td>
</tr>
<tr>
<td>1.11$^d$</td>
<td>32 (21–45)</td>
<td>95 (89–98)</td>
<td></td>
</tr>
<tr>
<td>$\beta_2$-MG, mg/L</td>
<td>0.899 ± 0.025</td>
<td>29 (21–39)</td>
<td>97 (93–99)</td>
</tr>
<tr>
<td>3.09$^b$</td>
<td>29 (21–39)</td>
<td>97 (93–99)</td>
<td></td>
</tr>
<tr>
<td>1.66$^c$</td>
<td>95 (88–98)</td>
<td>47 (40–54)</td>
<td></td>
</tr>
<tr>
<td>3.30$^d$</td>
<td>35 (26–45)</td>
<td>95 (91–98)</td>
<td></td>
</tr>
<tr>
<td>Creatinine, μmol/L</td>
<td>0.840 ± 0.031</td>
<td>85.9$^b$</td>
<td>29 (21–39)</td>
</tr>
<tr>
<td>47.7$^c$</td>
<td>95 (88–98)</td>
<td>47 (40–54)</td>
<td></td>
</tr>
<tr>
<td>83.0$^d$</td>
<td>35 (26–45)</td>
<td>95 (91–98)</td>
<td></td>
</tr>
<tr>
<td>Schwartz formula, mL/min</td>
<td>0.917 ± 0.018</td>
<td>56.0$^b$</td>
<td>31 (21–39)</td>
</tr>
<tr>
<td>93.6$^c$</td>
<td>95 (88–98)</td>
<td>65 (58–71)</td>
<td></td>
</tr>
<tr>
<td>70.8$^d$</td>
<td>68 (56–78)</td>
<td>95 (91–98)</td>
<td></td>
</tr>
</tbody>
</table>

$^a$ Data (with 95% confidence intervals in parentheses) result from ROC curve analysis performed with 150 children with a GFR >90 mL · min$^{-1}$ · 1.73 m$^{-2}$ and 75 children with GFR <90 mL · min$^{-1}$ · 1.73 m$^{-2}$.

$^b$ Upper cutoff limit (97.5% percentile); lower cutoff limit (2.5% percentile) in the case of the Schwartz GFR (see Table 1).

$^c$ Threshold with diagnostic sensitivity of 95%.

$^d$ Threshold with diagnostic specificity of 95%.

### Discussion

The identification of patients with mildly impaired GFR in the so-called “creatinine-blind” area remains a challenge for pediatric nephrologists. Although inulin clearance is the gold standard (20), GFR determination in children is barely practicable because timed urinary sampling is unreliable in children. Therefore, most pediatric centers use a single-shot, nuclear medicine clearance, either $^{99m}$Tc-DTPA (13) or $^{51}$Cr-EDTA (14).

Serum creatinine is a crude marker of GFR, especially in children. In our experience with renal transplants, a change in serum creatinine from 24 to 40 μmol/L within the reference interval reflects ~50% decline in GFR. Serum creatinine typically varies slightly from day to day (21), but age- and gender-associated differences in creatinine production are proportional to muscle mass, and creatinine generation can vary significantly in a given individual over time when muscle mass changes (22, 23). Tubular secretion of creatinine varies not only within an individual but also between individuals, and the proportion of total renal creatinine excretion attributable to...
The latter further amplifies the overestimation of GFR, which creatinine clearance represents (24). The significant age dependency of serum creatinine, although often forgotten, has been addressed by the use of height/creatinine ratios (1, 25); however, even these results may be misleading in children with a very low muscle mass. Serum creatinine, however, is rarely reported with the height/creatinine ratio even in dedicated pediatric hospitals. In our study, with the use of enzymatically determined serum creatinine and the factors 38 for children >1 year and 48 for adolescent males [Schwartz estimate (17) with a 20% correction for enzymatic measurement of creatinine], there was a reasonably good correlation between the nuclear medicine clearance and the estimated GFR (r = 0.706, P < 0.0001). However, a marker independent of age and gender would be preferable.

Both β2-MG (26) and Cys-C [reviewed in Ref. (4)] have the advantages of age and muscle mass independence (3, 27). BTP was introduced recently as a novel marker for measurement of kidney function in the creatinine-blind range (8, 10). In comparison with serum creatinine, all three low-molecular weight proteins, Cys-C, β2-MG, and BTP, have been reported to have a better diagnostic sensitivity for detection of impaired GFR (10, 27, 28). β2-MG has the disadvantage of being increased in patients with several malignancies and infectious diseases, particularly lymphoproliferative disorders (29). Apart from these interferences, serum concentrations of low-molecular weight proteins will be primarily determined by GFR, and an ideal marker has to have a constant production rate and should not vary in its concentration in situations with an acute-phase reaction. BTP seems to share these properties. That Cys-C is independent of age and gender is well established (5, 6, 30). Here, we demonstrate that BTP, like Cys-C, is independent of age and gender. Therefore, age- and gender-independent upper limits in our control group with GFR values >90 mL·min⁻¹·1.73 m⁻² could be calculated. The upper reference limits (parametric 97.5 percentiles) of serum BTP and Cys-C were 1.01 and 1.20 mg/L, respectively. For BTP, a mean value of 0.46 ± 0.13 mg/L was found in adults, using the same assay (10). The cutoff for Cys-C roughly corresponds to reference intervals shown in other pediatric studies (6, 27, 31–35). Slight differences may reflect assay differences (turbidometric or nephelometric assay) and/or the use of different calibrators (34, 36).

Similar to the findings in adults (4, 10), we found that the ROC plot area of serum creatinine was worse than that of both Cys-C and BTP (Table 2), but the areas for the two proteins were not significantly different (P > 0.05). The upper reference limits of both BTP and Cys-C predicted reduced GFR more sensitively than did those of creatinine or β2-MG (Table 2). These Cys-C data correspond to the promising results reported in other recent pediatric studies (37, 38), although earlier studies, including our own (5, 34), did not demonstrate such a distinct improvement of sensitivity. Because BTP is equivalent to Cys-C determination as a sensitive predictor of reduced GFR, this new low-molecular weight protein could be considered to replace creatinine or to be used in combination with creatinine as discussed in the case of Cys-C (34, 39, 40). Further studies have to show whether extrarenal causes, such as malignancies or treatment with glucocorticoids, increase serum BTP without evidence of impaired GFR, as was found for Cys-C (41, 42).

We found a significant difference in the diagnostic efficiency of the height/creatinine ratio when compared with creatinine using age-dependent reference values (7). Although it is well established that the Schwartz formula overestimates the GFR in patients with a GFR <15 mL·min⁻¹·1.73 m⁻², the overestimation in patients with a GFR >90 mL·min⁻¹·1.73 m⁻² is negligible and was 10.3% ± 3% when the GFR was >50 mL·min⁻¹·1.73 m⁻² (43). This study confirms that a height/creatinine ratio provides a better way of estimating GFR in healthy and mildly impaired renal function when compared with age-dependent creatinine reference values. In addition, one can conclude from the diagnostic validity data summarized in Table 2 that BTP and Cys-C were not significantly different from the height/creatinine ratio clearance estimate for the detection of impaired GFR, and therefore, the higher costs are not justified. However, there is a well-known problem with increased muscle mass in male adolescents. Schwartz et al. (17) recognized this fact and adjusted the constant accordingly in that age group. Although it would be preferable to have a marker that is independent of such influences, because puberty can occur prematurely or be delayed in some males, our
results also show that the Schwartz formula is sufficiently able to compensate for the age and muscle mass effects.

In summary, this study showed that the low-molecular weight serum proteins BTP and Cys-C had higher diagnostic accuracy than serum creatinine for identification of moderately impaired GFR in children, but they did not yield better diagnostic accuracy than the Schwartz GFR estimate.

We thank Dade Behring for providing us with Cys-C and BTP test methods free of charge. This work was partly supported by grants from the Humboldt University, Berlin.

References


