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Letter to the Editor

Reply to "Accuracy of determination of free light chains (Kappa and Lambda) in plasma and serum by Swedish laboratories as monitored by external quality assessment"

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To the Editor,

In their recent study, Rollborn et al. showed that an external quality assurance (EQA) program provides a valuable tool to monitor differences between serum free light chain (sFLC) methods over time [1]. The authors demonstrated that the combination of both reagents and instrument platforms affects sFLC quantification and may result in clinically relevant differences in reported FLC-ratio. To study the consistency of differences between FLC-methods over the period of 2015–2020, the authors exclusively selected samples from patients without monoclonal gammopathies. This harmonization step gives rise to samples with polyclonal FLC that can be measured at default dilution, which excludes the influence of non-linearity as a potential source of bias.

Despite this harmonization step, it is important to note that in this study unique samples are prepared for each EQA round which introduces the possibility that differences in FLC-results might not reflect inconsistencies in FLC-method performance but rather actual differences in the samples themselves. A well-known phenomenon in this context is that Freelite (The Binding Site, Birmingham, England) has adjusted FLC-ratio reference ranges for patients with renal impairment, while N Latex FLC-ratio (Siemens Healthineers, Munich, Germany) is not affected by kidney function [2]. Although not fully understood, it may for a large part be explained by two different observations. First, FLC can dimerize and FLC monomer–dimer patterns are different between patients and healthy controls [3]. Second, recently Caponi et al. showed that FLC-measurements are influenced by the FLC-polymerization status with striking differences in the reactivity of Freelite and N Latex reagents to either FLC dimers or FLC monomers [4]. Within the Dutch EQA program we have previously distributed a serum sample from a patient with chronic kidney disease without a monoclonal gammopathy. Fig. 1 indeed illustrates the strong difference between the average Freelite FLC-ratio (1.55, n = 25) and the average N Latex FLC-ratio (1.04, n = 7), which is completely in line with current literature [2,5].

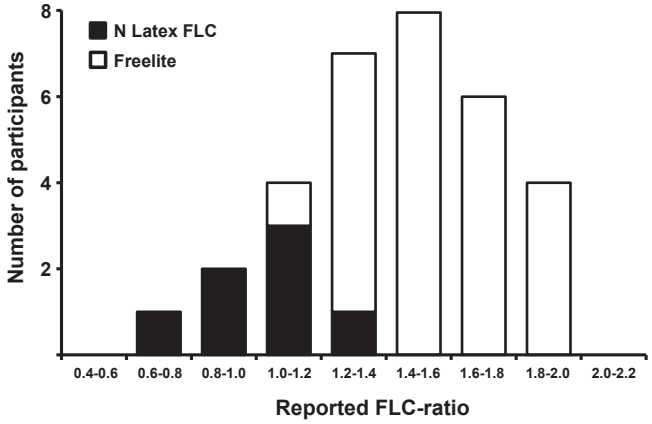

Fig. 1. FLC-ratio in EQA sample derived from patient with chronic kidney disease. Histogram showing the reported FLC-ratios of 32 participants in the Dutch EQA program analyzing a serum derived from a patient with renal impairment and no monoclonal gammopathy. Black bars represent participants who make use of N Latex FLC reagents (n = 7) and white bars represent participants using Freelite reagents (n = 25).

In their publication, Rollborn et al. do not provide information whether their EQA samples with elevated C-reactive protein could have been derived from patients with renal impairment. In that case some of the discrepancies between FLC-results would not be caused by an instability of the FLC-methods, but in fact reflect the structural difference in performance of these FLC-reagents in patients with renal impairment. Because the impact of renal impairment is different between the various commercially available FLC-assays (including different reference ranges), EQA schemes for FLC-testing should indicate whether samples are derived from individuals with renal impairment.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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