Letter to the Editor

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Reply to: Spurious results for total and free prostate-specific antigen (PSA); sometimes really "a riddle wrapped in a mystery inside an enigma"

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To the Editor,

Dorizzi et al. [1] reported a relevant clinical case on the aberrant free/total prostate specific antigen (fPSA/tPSA) percentages increasing over 100% and on the discrepant results of tPSA and fPSA obtained from different assays. We agree with the authors that these cases should be deeply investigated and reported in literature since actually uncommon. We should remind that in these rare cases the measurement of the biomarkers results in an unfavourable risk-benefit and cost-effectiveness ratio for the patient and the healthcare systems respectively. Indeed, as described in this case, more investigations (i.e. biopsy, magnetic resonance imaging, additional PSA measurements…) are required to try to explain the aberrant fPSA/tPSA ratios which cause a further increase of the health care costs and worsen the quality of life of the patient [2]. The interplay between laboratory professionals (as described in this case), urologists and manufacturers is therefore needed to increase the knowledge, share the evidence and finally improve the technology. We should remind that these efforts are made in order to restore the benefit of biomarker evaluation on healthcare and patient. In our opinion the stewardship of laboratory professionals is not affected by the lack of indication of the immunoassay used for PSA testing in the laboratory report but by the lack of knowledge on the state of harmonization of PSA immunoassays and the lack of a clinical-laboratory interface [2, 3]. The state of harmonization is undoubtedly suboptimal for tPSA methods (inter-assay coefficient of variation (CV)=11.5%) but really poor for fPSA (inter-assay CV=20.4%) methods, considering however that these results have been generated in a screening context characterized by a lowest risk of having aberrant results as those reported in this case [4, 5]. We will cautionary consider the cross-reactivity with human kallikrein (hK2) of Roche assay as possible explanation of these aberrant results between Beckman and Roche immunoassays, as reported by Dorizzi et al. [1], since a relevant (and possibly interfering) increase of hK2 may be detected in patients with high grade tumors and this is not the case [6, 7]. We encourage the use of other technologies (i.e. mass spectrometry) as an aid to investigate the presence of isoforms that may be recognized by fPSA immunoassays and cause spurious increases [8]. In conclusion, this case report [1] may be considered a good example of laboratory stewardship further encouraging to invest on more research towards fPSA and tPSA assay harmonization. It reminds that post-market assessments are needed for improving the cost-effectiveness of laboratory testing and practice.

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