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The improvement of turnaround-time (TAT) is one of the major objectives of laboratories to meet the expectations of clinicians while ensuring high quality of results. Pre- and post-analytical phases were found to contribute approximately 75% to the total TAT [1] for routine inpatient samples. However, for stat samples, the TAT was 1 h with pre- and post-analytical phases of 50%. According to Goswami et al., the streamline of the pre- and the post-analytical phases greatly improved the TAT. In addition, pre-analytical phase, specially the centrifugation conditions, are critical step for the quality of the biological results. Indeed, during centrifugation, the temperature and the speed as well as collection tube are crucial to preserve the integrity of samples, each change of one of these conditions may alter the plasma/serum quality and therefore laboratory results.

We aimed to evaluate the impact of 3 centrifugation protocols on plasma quality and analytical results of 8 routine biochemical parameters, measured in Lithium heparin (Lihep) tubes.

A total of one hundred triple samples on Lihep tubes (BD Vacutainer Lithium heparin REF 368886, 6 mL, 13 × 10 mm) delivered to our laboratory, were used in this study. Among these triple samples, only one tube was requested for routine lab (Tube A) while two additional tubes were in excess (Tubes B and C). The tube A (protocol A) was considered as the reference using routine lab condition i.e 2000g for 10 min (T10/2000). The tubes B and C (protocols B and C) were centrifuged at 3000g for 5 min (T5/3000) and at 4000g for 3 min (T3/4000), respectively (Figure A). All centrifugations were performed on Heraeus Multifuge X3FR centrifuge (ThermoScientific, Illkirch, France). The three tubes A, B and C were centrifuged in parallel according to their respective protocols A,B,C. Immediately, after centrifugation, tubes were decapped, and eight parameters were measured on Cobas 8000 analyzer (Roche Diagnostics, Meylan, France) including emergency, hemolysis sensitive and immuno-analysis parameters i.e Aspartate aminotransferase (AST), bilirubin, ferritin, human chorionic gonadotropin (hCG), high-sensitivity cardiac troponin T (hs-cTnT), lactate dehydrogenase (LD), Potassium and thyroid-stimulating hormone (TSH). Plasma quality was assessed by hemolysis/icterus/lipemia-indices (HIL) determination on Cobas 8000 and platelet count was determined on Pentra ES60 (Horiba®ABX SAS, Montpellier, France). The protocol A was called 'TO Ref' (baseline). To assess the acceptability

of B, C centrifugation protocol, we compared results from the protocol A with both other conditions using Passing Bablok regression. We reported the optimal allowable error (OAE) based on EFLM Biological variability database [2], except for the hCG and ferritin for which we used Ricos database [3] and we calculated the reference change value (RCV) as well as the total change limit (TCL) described by Oddoze et al. [4]. If the mean percentage deviation was higher than the OAE, RCV and TCL values calculated for each analyte, the centrifugation condition was considered unacceptable, i.e not usable in routine.

The median values for the eight parameters studied through the three centrifugation protocols were comparable with no statistically significant differences. The mean difference (%) between different centrifugation conditions (T10/2000g vs T5/3000g and T10/2000g vs T3/4000g) not exceeded the OAE, the RCV, TCL of each analyte (Table A).

The Passing Bablok regression demonstrated a good correlation and the three protocols may be used interchangeably for all tested biochemistry parameters (Fig. 1). However, since the majority of HCG values were <5 UI/L, the influence of the centrifugation conditions should be taken with caution given that the entire measurement range was not represented. Comparing the percentage of samples below the lower clinical cutoff, no significant differences were observed (Table B).

In Figure B, the variation of presence of hemolysis or number of platelets, demonstrated that a rapid centrifugation protocol didn't alter the plasma quality, with even an improvement, as a trend to a reduced number of platelets was observed below 20×10^9 PLT/L with a median of 14, 2 and 3×10^9 PLT/L for protocols A, B and C, respectively. For hemolysis, the same order of data was obtained with HI below 4 mg/dL, with a median of 0.1, 3 and 1 mg/dL according to protocols A, B or C, respectively. The low variation between the different centrifugation conditions, was not significant, remaining far from 10 mg/dL. None variation was observed for icterus and lipemia indexes, unlike to the study of Koenders et al. [5].

Our study reported that the rapid centrifugation of samples (protocols B or C) would seem to preserve sample quality and provide comparable values for eight biochemistry analytes tested versus standard centrifugation. Consequently, the centrifugation time in Lihep samples can be down-scaled from 10 min to 3 min at 4000g without affecting the analytes studied. Effectively, AST, potassium, and LD are

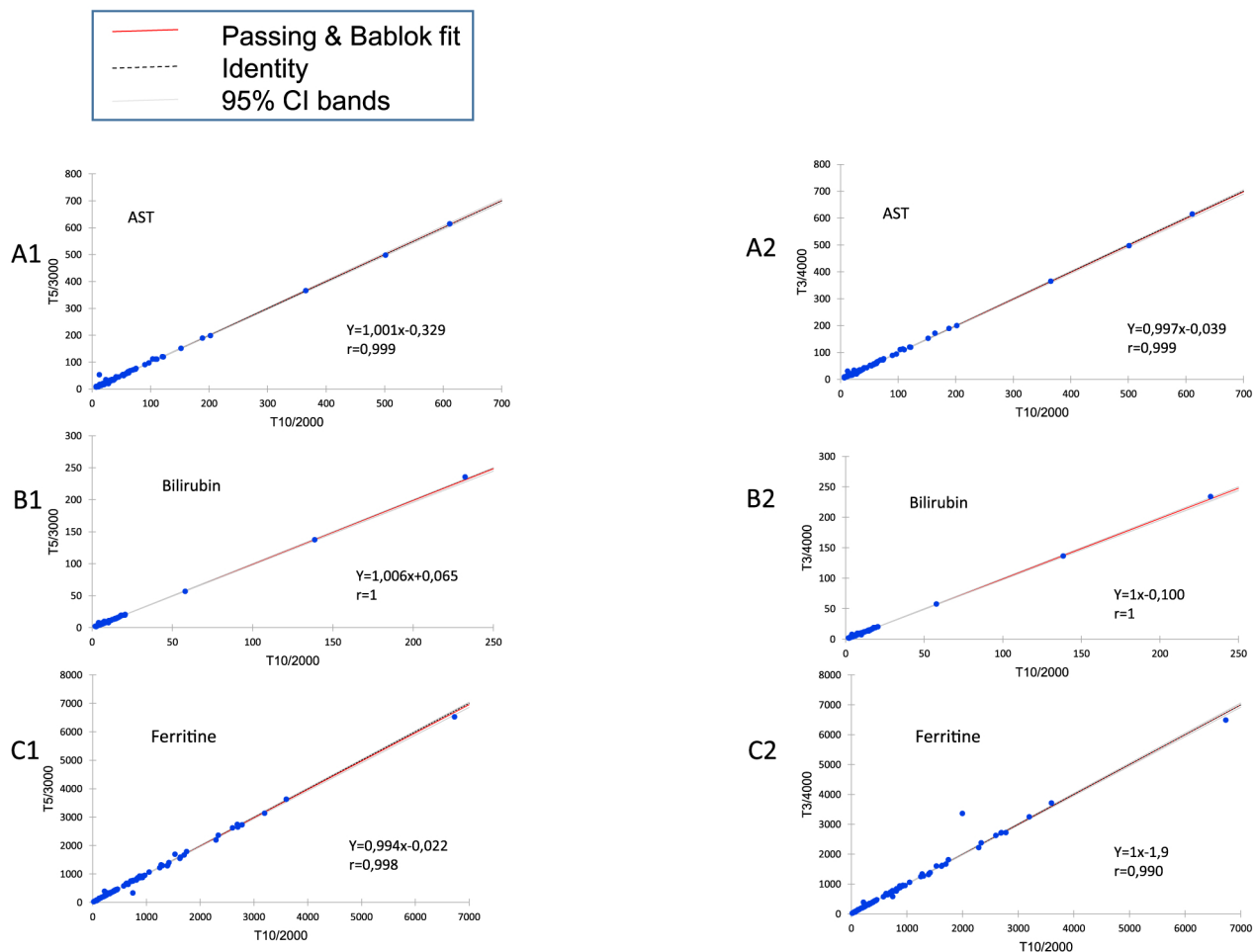


Fig. 1. Passing-Bablok regression analysis on plasma samples ($n = 100$) of eight parameters with conditions of centrifugation of 2000g for 10 min (T10/2000) vs 3000g for 5 min (T5/3000) (A1, B1, C1, D1, E1, F1, G1, H1) and of 2000g for 10 min (T10/2000) vs 4000g for 3 min (T3/3000) (A2, B2, C2, D2, E2, F2, G2, H2) AST: Aspartate aminotransferase; hCG:human chorionic gonadotropin; hs-cTnT: high-sensitivity cardiac troponin T; LD: lactate dehydrogenase; TSH: thyroid-stimulating hormone.

very sensitive to cellular influence and are present in red cells in higher concentrations than in plasma, so according to Dimeski 'study [6] these parameters as well as the platelets counts are suitable to ensure the highest sample quality. A compilation of studies reporting centrifugation conditions impact on the biochemistry test results was reported in additional file (Table C). Overall, all studies provided good correlation between results obtained with their standard centrifugation condition (2000g/10 or 15 min) and the tested centrifugation condition with a shortened centrifugation time (7 min, or 5 min or 3 min) at higher g-forces (3000g, 4000g or 6000g).

In addition, overall the rapid centrifugation of blood samples improves the sample quality [7] even if an increased HI was observed [5]. Although some studies suggest that rapid centrifugation should be done with caution to the LD and lipemia index [5,8,9], no impact on LD value and lipemia index was observed in our study.

The improvement of TAT without affecting sample quality is of great interest for laboratories and for the reporting of results to clinicians as early as possible. Since the centrifugation is time-consuming step in sample processing, the shortened time of centrifugation is mandatory. We believe that our results in accordance with previous studies, allow to justify the use of rapid centrifugation on Lihep plasma for routine biochemistry tests. A same approach was undertaken for the coagulation factors as previously published [10]. This is particularly relevant because the tendency in the field of biological laboratory is the centralization of analysis on automated platforms requiring an

optimized protocol of centrifugation to avoid slowing the throughput.

The data reported in this study, could allow a reduction of centrifugation-time from 10 min to 5 or 3 min for all Lihep samples, yielding a theoretical benefit at least of 5 to 7 min in intra laboratory TAT. Previously, we showed that the use of low vacuum BD Barricor™ tube in ED reduce hemolysis and also lab TAT due to a shortened centrifugation time (3 min at 4000g), as other report [11]. So, the protocol of 4000g for 3' appears suitable for all type of Lihep samples leading to the simplification of a critical pre-analytical step and would allow a substantial improvement in TAT.

In conclusion, our study demonstrates that a rapid centrifugation has no impact on the concentrations of the eight tested biochemistry parameters, which should reduce the TAT of clinical biochemistry tests while preserving a high sample quality. Nevertheless, as a large number of factors may influence the sample quality, each laboratory should validate its centrifugation protocol.

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.

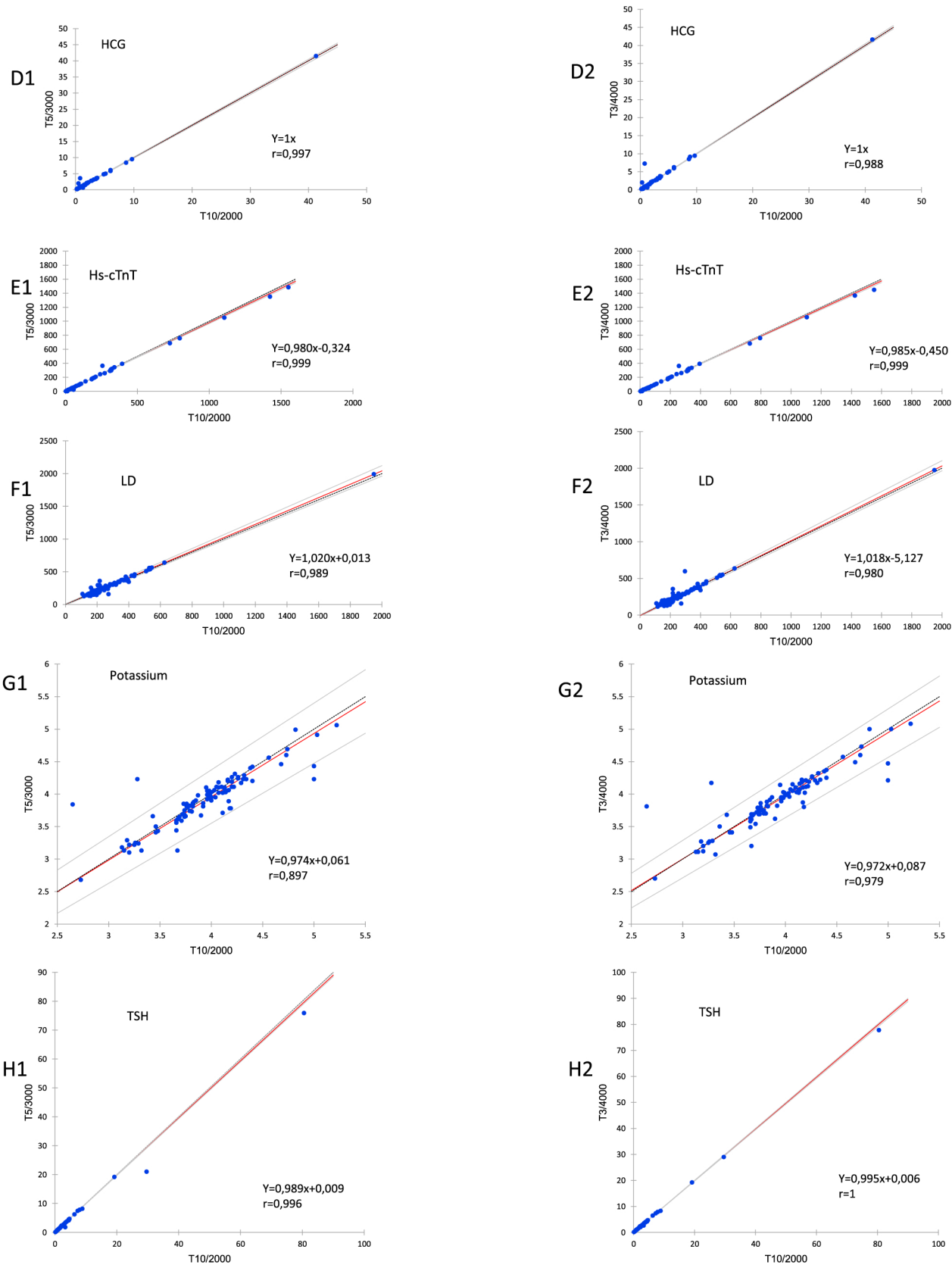


Fig. 1. . (continued).

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