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Determination of cardiac troponin I - modern solutions to improve diagnostic and clinical management in patients with suspected acute coronary syndrome

SUMMARY

Introduction: One of the biggest challenges in the laboratory diagnosis of cardiovascular diseases are acute coronary syndromes (ACS). It is estimated that every 10th patient admitted to hospital emergency departments (ED) has symptoms suggesting an acute myocardial infarction (AMI). Therefore, it is reasonable to use rapid strategies to rule out AMI based on high-sensitivity cardiac troponin I (hs-cTn) concentrations. The use of fast diagnostic and clinical algorithms in ED patients requires optimization of turnaround time (TAT). The most effective solutions to shorten TAT in routine laboratory practice can be introduced in the pre-analytical phase, which include the use of appropriate tubes such as BD PSTII™ and BD Barricor™ containing lithium heparin as an anticoagulant. BD Barricor™ tubes have an innovative mechanical separator which allows to reduce the time needed for centrifugation by as much as 7 minutes compared to BD PSTII™ tubes. An important factor affecting the quality of laboratory tests and TAT are analytical interferences, including the most common hemolysis, which assessment in plasma or serum can be expressed using the hemolysis index (HI) which is available on automated biochemical-immunochemical systems.

Aim: The aim of the study was to assess the impact of modern laboratory solutions on the diagnostic and clinical management of patients with suspected ACS. This was achieved by evaluating: i) the occurrence of hemolysis in the BD Barricor™ and BD PSTII™ tubes, as quantified by the hemolysis index (HI) on the Atellica CH and Alinity c measurement systems; ii) impact of the use of BD Barricor™ and BD PSTII™ tubes on hs-cTnI concentration on the Atellica IM and Alinity i systems; iii) comparison of hs-cTnI methods on both systems and in both tubes, and iv) assessment of the impact of BD Barricor™ and BD tubes PSTII™ on AMI rule-out strategy using predefined cutoff values for hs-cTnI on Atellica IM and Alinity i analysers.

Material and Methods: The study was divided into an analytical and clinical part. The material in the analytical part consisted of 359 paired BD Barricor™ and BD PSTII™ tubes taken from patients hospitalized at the A. Jurasz University Hospital (SU) No. 1 in Bydgoszcz. The clinical part included 599 unselected patients admitted to the ED at the SU No. 1 in Bydgoszcz, with suspected AMI, in whom the duration of chest pain did not exceed 6 hours from admission to the ED. Blood was collected from each enrolled patient in BD Barricor™ and BD PSTII™ tubes. In both tubes, the HI was measured and hs-cTnI concentrations were determined on the Atellica and Alinity measuring systems within 30 minutes of centrifugation. A strategy based on a single measurement of hs-cTnI was used to exclude AMI using predefined cut-off points i.e. <4 ng/L for Alinity i and <5 ng/L for Atellica IM, respectively. The primary endpoint was to compare the effectiveness of the above-mentioned strategy to rule out AMI using BD Barricor™ tubes versus BD PSTII™ tubes.

Results: No between-tubes differences were observed in the incidence of high-grade (H3+) hemolysis [free hemoglobin (fHb) ≥2.00 g/L] and moderate-grade (H2+) hemolysis (fHb ≥1,00 g/L) regardless of the measurement system used. Statistically significant differences occurred in the detection of low-grade hemolysis (H1+) defined by fHb concentration ≥ 0.25 g/L. These included a lower incidence of H1+ on the Atellica CH analyzer in BD Barricor™ tubes compared to BD PSTII™ tubes (21.7% vs. 30.6%, p=0.007). In addition, a higher rate of H1+ detection in BD PSTII™ tubes was demonstrated on the Atellica CH compared to the Alinity c (30.6% vs. 22.3%, p=0.011).

The influence of both tubes on hs-cTnI results measured on both analyzers was also compared in the full measuring range (3-15000 ng/L) and in the lower measuring range of 3-300 ng/L. Based on the Deming regression equations and the correlation coefficient, no influence of the tubes on the obtained hs-cTnI results was demonstrated, regardless of the measurement system. The Deming regression equations and the corresponding correlation coefficients obtained between hs-cTnI methods on both analyzers in both tubes were also compared in the full measuring range of hs-cTnI and in the lower measuring range of hs-cTnI. The obtained values of the regression coefficients were lower than 1, which proves that hs-cTnI methods are not equivalent despite their high correlation (correlation

coefficient values ranged from 0.88 to 0.96) regardless of tubes and measurement range. Bland-Altman difference analysis showed that hs-cTnI concentrations obtained on the Alinity analyzer were lower than those obtained on the Atellica IM by an average of 38% to 40%, regardless of the type of tubes. In the clinical part, 599 subjects were included in the study and a rapid AMI rule-out algorithm was used based on a single measurement of hs-cTnI in both tube and analytical systems. Using this strategy, AMI was excluded in 530 patients after a single measurement of hs-cTnI, where the TAT was less than 1 hour. Finally, AMI was diagnosed in 69 patients, which accounted for 11.5% of all patients included in the study. The average age of the study population was 68.7 years and the majority were men. Patients with AMI did not differ in terms of age from those in whom AMI was excluded. AMI was significantly more often diagnosed in men than in women ($p<0.001$). The rapid AMI rule-out strategy applied in this study was characterized by an excellent diagnostic sensitivity and negative predictive value (NPV), regardless of the tube and analyzer used. Diagnostic sensitivity and NPV for Alinity and both tubes was 100%; diagnostic sensitivity for Atellica IM and both tubes was 98.6 %, NPV of Atellica IM in BD Barricor™ tube was 98.1% and in the BD PSTII™ was 98.2%, respectively. The lower diagnostic sensitivity and NPV values obtained in both tubes on the Atellica IM in comparison to the Alinity are due to the two false negatives, one per each tube. It was also shown that the presence of hemolysis had no effect on the rapid AMI rule-out strategy. In addition, the type of tube did not affect the classification of results below the defined cut-off values for hs-cTnI concentrations on both analyzers. Acceptable agreement has also been demonstrated for hs-cTnI results obtained in BD Barricor™ and BD PSTII™ tubes on the same measuring system.

Conclusions: BD Barricor™ and BD PSTII™ tubes have comparable analytical and clinical value, suggesting their interchangeable use on the Atellica IM and Alinity i hs-cTnI measuring systems. The use of BD Barricor™ tubes on both analyzers can significantly reduce TAT without negative impact on the sample quality and clinical value of results. Hs-cTnI results on both Atellica IM and Alinity analyzers are characterized by a significant systematic difference regardless of the tube type used, and these methods cannot be used interchangeably. The AMI rule-out strategy based on a single measurement using very low hs-cTnI concentrations in patients with suspected AMI was characterized by high diagnostic efficacy.