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LETTER TO THE EDITOR



4Ts Score and EuroSCORE in cardiac surgery 2

Anna Vittoria Mattioli¹ · Antonio Manenti¹ · Alberto Farinetti¹ З

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6 Dear Sir,

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7 We have read with great interest the paper "Initial and long 8 term impact of a multi-disciplinary task force in the diagno-

9 sis and management of Heparin-Induced thrombocytopenia" 10 by Lim et al. [1] and we found their conclusion of impor-11 tance with a view to clinical prevention.

12 The authors underline how diagnosis and management of 13 HIT has been changed after a retrospective audit on patients 14 who underwent at least one laboratory testing for HIT.

15 The audit demonstrated a high frequency of PF4-ELISA 16 testing (n = 54, 66%) in patients that had low 4T scores. 17 Also, a very low percentage of PF4-ELISA-positive cases 18 were confirmed to be SRA positive. If the 4T scoring criteria 19 were initially used prior to PF4-ELISA testing, 54 (65.8%) 20 PF4-ELISAs and 24 (55.8%) SRAs would not have been 21 performed, resulting in a cost savings of \$11,850 [2].

22 On the basis of these data, Authors evaluated the initial 23 and long-term impact and challenges of these institution-24 wide changes in the diagnosis and management of HIT in 25 the inpatient setting at an academic medical center. They 26 concluded that, despite their efforts, the number of PF4-27 ELISA testing was already higher than other academic medi-28 cal centers of similar size [1]. In order to reduce test and to 29 decrease costs they plan to create an electronic order set for 30 4T score for ELISA-PF4 testing.

31 With reference to the findings reported in the paper, we 32 would like to make the following contribution to the discus-33 sion. We refer the results of our retrospective analysis in 34 post-cardiac surgery patients about the incremental value 35

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of 4Ts Score and EuroSCORE for prediction of heparininduced thrombocytopenia.

The analysis was performed in a group of patients treated with unfractionated heparin undergoing cardiac surgery. Anti-PF4/heparin antibodies were tested in all patients using a commercial immunoassay (Asserachrom H PF4 ELISA kits) [3-5]. Of the 600 patients investigated, 131 (21.8%) were found to have anti-PF4/heparin antibodies in the postoperative period (5-7 days from surgery). All patients had the EuroSCORE [6] value and the 4Ts Score [7] evaluated before surgery As expected the 4Ts Score identify as high probability patients that developed antibodies and we found 22 thrombotic events (16.79%). Within the group of patients that tested negative to anti-PF4/heparin antibodies, the incidence of thrombotic complications was lower (5%)(p > 0.01).

A 4T Score > 3 identified medium and high risk and predicted an increased risk of thrombosis in patients independently of the EuroSCORE value and add information for stratification. In these patients the ELIZA test is suggested in order to identify the presence of antibodies. This group had a greater prevalence of antibodies and a greater prevalence of thrombotic complications at 30 days.

A low EuroSCORE value was associated with an exceedingly low hard-event rate (0.4% year) that increases significantly as a function of the 4T's score results. The 4Ts Score yielded incremental value for the prediction of hard events (X 56-88, p < 0.001) and significantly stratified patients. In patients with intermediate to high likelihood of complications as predicted by EuroSCORE the 4Ts Score significantly increased the prediction of events.

Our results suggested that cardiac surgery patients are at high risk for coagulation adverse effects, among which the generation of anti-PF4/heparin antibodies. This usually causes a late post-operative thrombocytopenia, and, when persisting, thrombotic complications at different levels [8-10].

The evaluation of the risk of patients had to include the 4Ts Score and the EuroSCORE in order to identify patients more likely to developed anti-PF4/heparin antibodies and

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- 75 thrombotic complications. These patients need a more
- ⁷⁶ careful follow-up and the ELISA test for anti-PF4/heparin
- antibodies could help in the management of post-operative
- ⁷⁸ anticoagulant therapy. On the other side patients with low
- risk could avoid PF4/ELISA test. We support the hypothesis
- 80 by Lim et al. that a HIT task force can reduce the number
- 81 of inappropriate HIT testing with significant cost savings.

82 Compliance with ethical standards

- 83 Conflict of interest Anna Vittoria Mattioli, Antonio Manenti and Al 84 berto Farinetti declare that they have no conflict of interest.
- 85 Ethical approval All procedures performed in studies involving human
- participants were in accordance with the ethical standards of the insti tutional and/or national research committee and with the 1964 Helsinki
- declaration and its later amendments or comparable ethical standards.

89 Informed consent Informed consent was obtained from all individual90 participants included in the study.

91 References

- Lim MY, Foster J, Greenberg CS (2017) Initial and long term impact of a multi-disciplinary task force in the diagnosis and management of heparin-induced thrombocytopenia. J Thromb
 Thrombolysis. https://doi.org/10.1007/s11239-017-1592-z
- Pierce W, Mazur J, Greenberg C, Mueller J, Foster J, Lazarchick
 J (2013) Evaluation of heparin-induced thrombocytopenia (HIT)

laboratory testing and the 4Ts scoring system in the intensive care unit. Ann Clin Lab Sci 43:429–435

- 3. Mattioli AV, Bonetti L, Sternieri S, Mattioli G (2000) Heparininduced thrombocytopenia in patients treated with unfractionated heparin: prevalence of thrombosis in a 1 year follow-up. Ital Heart J 1:39–42
- Warkentin TE, Heddle NM (2003) Laboratory diagnosis of immune heparin-induced thrombocytopenia. Curr Hematol Rep 2:148–157
- Mattioli AV, Bonetti L, Carletti U, Ambrosio G, Mattioli G (2009) Thrombotic events in patients with antiplatelet factor 4/heparin antibodies. Heart 95(16):1350–1354. https://doi.org/10.1136/ hrt.2008.160549
- Nashef SAM, Roques F, Michel P, Gauducheau E, Lemeshow S, Salamon R, for the EuroSCORE study group (1999) European system for cardiac operative risk evaluation (EuroSCORE). Eur J Cardio-thorac Surg 16:9–13
- Lee Y, Weeks P, Gass J, Sieg A (2017) Evaluation of 4T's scoring system in the identification of heparin-induced thrombocytopenia in patients with mechanical circulatory support. Thromb Res 160:66–68. https://doi.org/10.1016/j.thromres.2017.10.017
- Mattioli AV, Bonetti L, Zennaro M, Ambrosio G, Mattioli G (2009) Heparin/PF4 antibodies formation after heparin treatment: temporal aspects and long-term follow-up. Am Heart J 157(3):589–595. https://doi.org/10.1016/j.ahj.2008.11.007
- Greinacher A, Selleng K, Warkentin TE (2017) Autoimmune heparin-induced thrombocytopenia. J Thromb Haemost 15:2099–2114
- Selleng S, Selleng K (2016) Heparin-induced thrombocytopenia in cardiac surgery and critically ill patients. Thromb Haemost 116(5):843–851

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