Dear Editor,

Luo and colleagues have recently published a study entitled “Role of mean platelet volume in differential diagnosis of adult-onset Still’s disease and sepsis” in Revista da Associação Médica Brasileira examining the role of mean platelet volume (MPV) to distinguish adult-onset Still’s disease (AOSD) from sepsis. This is a potentially impactful article, since AOSD can be difficult to distinguish from sepsis and other reactive conditions. In particular, the use of complete blood cell count (CBC) data, which is nearly universally available, can provide a cost-effective means to arrive at the correct diagnosis. The goals of this letter are to (1) compare Luo et al’s data to earlier work on this subject and (2) add additional comments regarding the clinical application of MPV.

We followed the guidelines for systematic reviews of diagnostic accuracy studies and PRISMA guidelines. Because this study used publicly available data, it did not require ethical board approval. We conducted an electronic search using Medline (PubMed interface), Scopus, and Web of Science using the keywords “MPV” or “mean platelet volume” AND “Still disease” OR “Still’s disease,” without restrictions. The date of the search was January 22, 2022. The titles and abstracts were screened, and the full-text articles were then obtained for all potentially relevant studies. After all relevant studies were identified, the reference lists from each paper were reviewed for potentially relevant studies and a search of the PubMed and Google Scholar databases for citations of each paper was conducted to identify additional eligible articles.

The included studies were assessed using a standardized data extraction form. The mean and standard deviation (SD) of MPV values were included in a meta-analysis, with the calculation of weighted mean difference (WMD) and its 95% confidence interval (95%CI) in AOSD patients versus patient cohorts with diseases clinically resembling AOSD. For studies where the mean value and SD were not reported, we used the model of Hozo et al. in order to determine the SD from the sample size, median value, and range. Statistical calculations were performed using Meta Mar (www.meta-mar.com, accessed date January 25, 2022). The quality of the included studies was assessed using the Newcastle-Ottawa Scale (NOS), with the articles independently assessed by each author. A final score for each paper was arrived at by consensus.

After a search of the databases, screening of results, and review of reference lists and citations, a total of five studies met selection criteria (see Table 1). The studies were conducted in China (four studies) and Turkey (one

Table 1. Characteristics of studies analyzing mean platelet volume in adult-onset Still’s disease.

| Study     | Year | Country | AOSD sample size | Control group(s), size and clinical features | Age (years, mean and range) | MPV, AOSD vs. disease control (fL) | Analyzer   | NOS |
|-----------|------|---------|------------------|---------------------------------------------|----------------------------|-----------------------------------|------------|-----|
| Ge et al.5 | 2021 | China   | 110              | 84, sepsis                                   | 36 (16–74)                 | 9.69±1.31 vs. 10.85±1.24          | Sysmex XE 2100 | 8   |
| Liu et al.7 | 2019 | China   | 82               | 48, sepsis; 76 healthy                        | 36 (18–74)                 | 9.8 ± 1.2 vs. 11.1 ± 1.1           | Sysmex XE 2100 | 8   |
| Luo et al.3 | 2021 | China   | 68               | 55, sepsis                                   | 33 (18–74)                 | 10.08±1.11 vs. 11.14±1.09         | Sysmex XE 2100 | 6   |
| Ulutas et al.8 | 2021 | Turkey  | 61               | 61, FMS                                      | 39 (19–73)                 | 8.3±1.2 vs. 9.3±1.0               | NS         | 8   |
| Zhang et al.1 | 2020 | China   | 91               | 89, FUO; 81 healthy                           | 32 (16–74)                 | 9.80±1.23 vs. 10.42±1.03          | Sysmex XE 2100 | 6   |

MPV: mean platelet volume; AOSD: adult-onset Still’s disease; NOS: Newcastle-Ottawa Scale; FMS: fibromyalgia syndrome; NS: not stated; FUO: fever of unknown origin.

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3Conflicts of interest: the authors declare there is no conflicts of interest. Funding: none.
4Received on February 10, 2022. Accepted on February 27, 2022.
The studies included data on 412 AOSD patients, with sample sizes varying between 61 and 110 subjects. The control populations included 337 patients with clinical features resembling AOSD, including sepsis (3 studies)\(^1\), fibromyalgia syndrome (1 study)\(^8\), and fever of unknown origin (1 study)\(^9\). A total of 157 healthy control subjects were included in two studies\(^7,9\). Four studies used CBCs performed on the Sysmex SE analyzer (Kobe, Japan)\(^1,6,7,9\); for the remaining study, the blood analyzer was not identified\(^4\). The standardized mean difference (SMD) for five studies is shown in Figure 1. Since heterogeneity (I\(^2\) statistic) was <50%, a fixed-effects model was used. MPV was found to be significantly higher in disease control patients compared to AOSD patients (SMD=0.85, 95%CI 0.7–1.0). The cumulative data thus support a potential role for MPV in the differential diagnosis of AOSD.

There are several points we would like to emphasize, in particular for clinicians and others interested in the use of MPV for clinical purposes and to assess the MPV as a potential biomarker in AOSD. First, although the quality of the studies was overall adequate or good, with NOS score ranging from 6 to 8, there was overall a lack of information about preanalytical phase variables that could potentially impact results. These variables include time between phlebotomy and analysis, choice of anticoagulant, and storage/transport conditions\(^10\). Researchers should control for these variables, and clinicians should be aware of these potential sources of bias. In addition, all studies that reported the hematology instruments used in obtaining the MPVs (n=4) used the same instrumentation platform (Sysmex XE, Sysmex). This potentially limits the generalizability of the data since there are continuing problems with cross-platform harmonization of the MPV\(^11\). Therefore, the reproducibility of these findings has not yet been established when other instrumentation platforms/methodologies are used. In addition, the difference in MPV between the Still's disease and control groups was on

![Figure 1](image-url)

**Figure 1.** Standardized mean difference (SMD) and 95% confidence interval (95%CI) of mean platelet volume values in patients with adult-onset Still’s disease versus control populations with symptoms suggesting Still’s disease.
average ~1 fL. Given the current limitations of the technology and potential problems with preanalytical and analytical variables, it would be difficult to meaningfully interpret individual patient results.

In summary, our analysis adds additional context to the paper by Luo et al that describe the potential role of MPV in AOSD patients. We again thank Luo et al for their addition to this evolving literature and hope that our comments are useful to the readership of Revista da Associação Médica Brasileira.

AUTHORS’ CONTRIBUTIONS
JLF: Conceptualization, Data curation, Formal Analysis, Methodology, Writing – original draft. CLS: Data curation, Formal Analysis, Writing – review & editing.

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