Myocarditis after vaccination against COVID-19: an umbrella review of systematic review and meta-analysis

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Introduction: A few months after the beginning of the COVID-19 vaccination, several reports of myocarditis secondary to the vaccines were published, sometimes with fulminant cases, but until today there is no proven causal link between these two events, but with many hypotheses proposed.

Purpose: We conducted an umbrella review of all systematic reviews with meta-analyses published in this sense, in order to carry out a critical review to be able to draw relevant conclusions for our practice.

Methods: A systematic review of current evidence regarding myocarditis after COVID-19 vaccination was performed by searching several databases including PubMed/Medline and Web of Science. The quality of MAs was assessed using the AMSTAR-2 tool as well as other qualitative criteria. The evidence was graded from convincing (Class I) to weak (Class IV), according to the type of studies included (prospective or retrospective), p-value of the overall effect, level of heterogeneity, sample size, or inclusion or not of the null value in the 95% confidence interval.

Results: Our umbrella review appraised 4 MAs of retrospective studies (range: 5–12). The number of vaccine doses included ranged from 12 to 179 million, with the number of myocarditis cases observed ranging from 343 to 1489. All types of vaccines were evaluated, with no exclusions. The overall incidence ranged from 0.89 to 2.36 cases of myocarditis per 100,000 doses of vaccine received (Figure 1). Heterogeneity was assessed in 3 of the MAs, and was highly significant (>75%) in all included studies, and with a significant p-value (p <0.05). Regarding publication bias, three of the MAs conducted the egger and begg regression, with a significant result in only one. Of the 4 MAs included, only one was not registered in the PROSPERO database. Writing guidelines and reporting, including Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA), were used in all included MAs. Regarding the assessment of the methodology by the AMSTAR-2 scale indicating that the quality was very critical in one, low in 2 MAs, and moderate in one MA. All MAs were classified as level IV evidence except one, which was classified as level III, and this was due to the retrospective nature of the included studies and the failure to report the p-value of the overall effect.

Conclusion: Despite the power of meta-analysis to increase sampling and precision, the quality of current non-randomized evidence on real causality and real incidence of myocarditis after COVID-19 vaccine is still low.