Red cell mass measurement is still useful for the management of myeloproliferative neoplasms. Comment to "Role of red cell mass evaluation in myeloproliferative neoplasms with splanchnic vein thrombosis and normal hemoglobin value: a study of the France Intergroupe des Syndromes Myeloprolifératifs"

We read with interest the study by Galtier *et al*. on the usefulness of red cell mass (RCM) measurement in patients with myeloproliferative neoplasms (MPN) with splanchnic vein thrombosis (SVT) associated with normal hemoglobin values, recently published in *Haematologica*.[1]

In the study, the authors investigate the impact of RCM evaluation on diagnosis and management in a large cohort of 71 *JAK2*V617F-positive patients with SVT and normal hemoglobin values. Surprisingly, according to RCM values, 40 (56%) patients were diagnosed with masked polycythemia vera (m-PV), whereas 31 (44%) had normal RCM. Except increased RCM values, no other parameter (including hemoglobin and hematocrit levels, erythropoietin level, *JAK2*V617F allele burden, histology criteria etc.) was able to differentiate m-PV from non m-PV, stressing the need for RCM evaluation in all *JAK2*-positive STV patients with normal hemoglobin values, particularly due to the importance of reducing RCM in m-PV patients compared with non PV patients. It is worth noting that only 25% of m-PV patients who had a second RCM evaluation after at least 1 year of cytoreductive treatment achieved a decrease <125% in RCM, suggesting that 75% of m-PV patients were undertreated.

The work by Galtier *et al*. has the merit of clearly demonstrating the usefulness of RCM measurement in both the diagnosis and management of m-PV, as previously suggested by Lamy *et al*. many years ago.[2] Indeed, only RCM makes it possible to distinguish MPN with m-PV from patients without PV, with the inherent therapeutic consequences. On the other hand, this report raises questions about current access to RCM measurement due to the abandonment of isotopic techniques in most Western countries following concerns about the use of isotopes in humans.

Fortunately, the carbon monoxide rebreathing method (CO-rebreathing), an older method based on hemoglobin's affinity for CO and used to evaluate RCM since the end of the 19th century[3] but sidelined by the use of isotopes, has recently reappeared with encouraging results.[4] The method consists of inhalation of a fixed and precise quantity of CO delivered by a machine approved in Europe for clinical use, with determination of CO-hemoglobin at different time points, enabling blood volumes to be calculated in less than 15 minutes.

Very recently, Oberholtzer *et al*. used this technique to evaluate red cell volume, plasma volume and blood volume in a large cohort of more 700 individuals, including 107 athletes, with interesting results, confirming that the CO-rebreathing test is a fast, non-invasive and reliable alternative approach to RCM evaluation.[5]

Moreover, another recent prospective bicentric study comparing RCM obtained by either the CO-rebreathing test or isotopic measurement in a population of 42 patients referred for suspected polycythaemia reported a sensitivity of 84% and a specificity of 71%, underlining the good reliability of the CO-rebreathing test in the evaluation of RCM.[6]

Furthermore, Galtier *et al*. noted that 75% of m-PV patients were undertreated. More specifically, after at least 1 year of cytoreductive treatment, the RCM was significantly decreased in only 25% of m-PV patients, underlying the usefulness of repeating the RCM evaluation several months after treatment initiation. Due to the scarcity of isotopic measurement in most Western countries, the CO-rebreathing test is particularly well-suited, since it can be readily accessible and performed very rapidly in a trained pulmonary function department. The results of the French study currently underway on the therapeutic management of MPN with SVT will confirm the value of measuring RCM in the follow-up of patients with a high risk of recurrence, and provide a clearer picture of its role.

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Disclosures

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Contributions

FG and NM wrote the manuscript and performed research. FG supervised the study.

Data-sharing statement

Data and detailed information related to the study are available from the corresponding author upon request.

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