Could Less Be Worth More?

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Short Editorial related to the article: Restrictive versus Liberal Transfusion Strategies in Acute Myocardial Infarction and Anemia: A Meta-Analysis and Trial Sequential Analysis

"For every complex problem there is a solution wich is clear, simple, and wrong"
Henry Louis Mencken

The use of biologically active products, such as stored blood, in the therapeutic arsenal generates controversy. With the development of hemotherapy, related complications, such as transfusion-transmitted infections, transfusion-related acute lung injury (TRALI), and severe hemolytic reactions, have become rare.[1,2] However, possible volume overload, with consequent pulmonary edema (transfusion-associated circulatory overload, TACO) and its clinical implications, is associated with a major cause of post-transfusion morbidity and mortality. Predisposing factors for the condition include ischemic cardiomyopathy and chronic kidney disease, often present in the context of acute myocardial infarction (AMI).[3,4]

Anemia can worsen myocardial ischemia in AMI, with an impact on mortality.[5] Two main strategies are present in clinical trials in the management of this condition: restrictive transfusion and liberal transfusion. The choice between these approaches remains a controversial topic, with critical implications for clinical practice and patient outcomes.

A study published in this issue of *Arquivos Brasileiros de Cardiologia*[6] presents careful meta-analysis and methodological considerations on the topic, revealing in a didactic and objective way how complex it is to identify a single strategy. From a systematic search on the main research platforms for randomized clinical trials (RCTs), comparing the two strategies in anemia associated with AMI, only three trials remained that met the eligibility criteria regarding the use of blood, efficacy, and safety (MINT,[7] REALITY,[8] and CRIT.)[9] With a total of 4,217 participants from the three RCTs followed for 30 days, no statistically significant difference was found between restrictive and liberal strategies in efficacy and safety outcomes. The authors highlight the possible impact of heterogeneity in treatment, clearly evident in the restrictive strategy. In REALITY, whose results suggested that the restrictive strategy was superior, the number of packed red blood cell units in the restrictive group was greater than in the liberal strategy.[8]

In the restrictive transfusion strategy, blood is only administered when hemoglobin levels fall below a specific threshold, which varies between 7 and 8 g/dL, with the hypothesis that reducing the use of transfusions can minimize risks and costs. In AMI, excessive transfusion can increase blood viscosity, potentially worsening myocardial ischemia and impairing recovery.

In the liberal transfusion strategy, blood is administered at higher hemoglobin levels, generally between 9 and 10 g/dL. The concept would be that maintaining higher levels of hemoglobin could improve tissue oxygenation and perfusion, especially in patients with AMI, where the demand for oxygen is critically high, and anemia can generate more hypoxia, with a worse prognosis. On the other hand, in clinical trials evaluating transfusion strategies for infarction, such as CRIT and REALITY, there was an increase in the number of cases of congestion in the liberal group compared to the restrictive group.[8,9]

Clinical guidelines, such as those from the American College of Cardiology (ACC) and the American Heart Association (AHA), tend to favor a more restrictive approach, emphasizing the need to individualize the transfusion decision based on the patient's clinical status, symptoms of anemia, and comorbidities. Showing how complex it is to assert a single conduct, the Reality study, which showed greater benefit with the restrictive strategy, had its results reversed after the fifth month. (HR 1.44, 95% CI 1.01-2.03 at one year). The advantage of the restrictive strategy in Reality in 30 days has not been confirmed in a year.[10]

The definition of what conduct to adopt remains current and controversial, with no definitive answer yet, which adds value to the work published here. As highlighted by the authors, different goals from the decision to transfuse are vague, and whether the objective was to "correct" hemoglobin to a pre-established level (>10) or even clinical stability. Such variation certainly harms and interferes with outcomes.

While current evidence favors a more restrictive approach in many cases, the final decision must be carefully personalized, taking into account the specific clinical condition and needs of the patient. The balance between minimizing risks and maximizing benefits remains the primary objective in managing these complex patients.

The well-conducted meta-analysis and the limitations pointed out by the authors highlight the need for future studies with well-defined populations and protocols. Until then, it is important to maintain individualized management, valuing the patient's clinical condition until the best evidence is available.

Keywords

Anemia; Blood Transfusion; Myocardial Infarction; Meta-Analysis

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References

1. Busch MP, Bloch EM, Kleinman S. Prevention of Transfusion-transmitted Infections. Blood. 2019;133(17):1854-64. doi: 10.1182/blood-2018-11-833996.
2. Toy P, Gajic O, Bacchetti P, Looney MR, Gropper MA, Hubmayr R, et al. Transfusion-related Acute Lung Injury: Incidence and Risk Factors. Blood. 2012;119(7):1757-67. doi: 10.1182/blood-2011-08-370932.
3. Narayan S, editor. The 2023 Annual SHOT Report. Manchester: Serious Hazards of Transfusion Steering Group; 2024.
4. Murphy EL, Kwaan N, Looney MR, Gajic O, Hubmayr RD, Gropper MA, et al. Risk Factors and Outcomes in Transfusion-associated Circulatory Overload. Am J Med. 2013;126(4):29-38. doi: 10.1016/j.amjmed.2012.08.019.
5. Mamas MA, Kwok CS, Kontopantelis E, Fryer AA, Buchan I, Bachmann MO, et al. Relationship between Anemia and Mortality Outcomes in a National Acute Coronary Syndrome Cohort: Insights from the UK Myocardial Ischemia National Audit Project Registry. J Am Heart Assoc. 2016;5(11):e003348. doi: 10.1161/JAHA.116.003348.
6. Fabiano RC, Melo L, Nogueira A, Gewehr DM, Generoso G, Cardoso R, et al. Restrictive versus Liberal Transfusion Strategies in Acute Myocardial Infarction and Anemia: A Meta-Analysis and Trial Sequential Analysis. Arq Bras Cardiol. 2024; 121(9):e20240158. DOI: https://doi.org/10.36660/abc.20240158i.
7. Carson JL, Brooks MM, Hébert PC, Goodman SG, Bertolet M, Glynn SA, et al. Restrictive or Liberal Transfusion Strategy in Myocardial Infarction and Anemia. N Engl J Med. 2023;389(26):2446-56. doi: 10.1056/NEJMoa2307983.
8. Ducrocq G, Gonzalez-Juanatey JR, Puymirat E, Lemesle G, Cachanado M, Durand-Zaleski I, et al. Effect of a Restrictive vs Liberal Blood Transfusion Strategy on Major Cardiovascular Events Among Patients with Acute Myocardial Infarction and Anemia: The REALITY Randomized Clinical Trial. JAMA. 2021;325(6):552-60. doi: 10.1001/jama.2021.0135.
9. Cooper HA, Rao SV, Greenberg MD, Rumsey MP, McKenzie M, Alcorn KW, et al. Conservative versus Liberal Red Cell Transfusion in Acute Myocardial Infarction (the CRIT Randomized Pilot Study). Am J Cardiol. 2011;108(8):1108-11. doi: 10.1016/j.amjcard.2011.06.014.
10. Gonzalez-Juanatey JR, Lemesle G, Puymirat E, Ducrocq G, Cachanado M, Arnaiz JA, et al. One-year Major Cardiovascular Events after Restrictive versus Liberal Blood Transfusion Strategy in Patients with Acute Myocardial Infarction and Anemia: The REALITY Randomized Trial. Circulation. 2022;145(6):486-8. doi: 10.1161/CIRCULATIONAHA.121.057909.