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Comparison of Serum and Cellular Methods for Disease Monitoring in Multiple Myeloma: Is it always necessary to perform both?

Ana Catarina Fonseca[1*], Patrícia Maia[1*], Carina Faria[1], Carla Azevedo[1], Julieta Silva[1], Andreia Pinto[1], Catarina Ferreira[1], Maria Emília Sousa[1], Carlos Palmeira[1,2,3,4,5], Paulo Silva[1], João Pedro Barreto[1], Bruno Fernandes[1], Gabriela Martins[1]

*These authors contributed equally to this work

1 Serviço de Patologia Clínica, Instituto Português de Oncologia do Porto Francisco Gentil, Porto, Portugal
2 Experimental Pathology and Therapeutics Group, Research Center of IPO-Porto (CI-IPOP), Porto, Portugal
3 RISE@CI-IPOP (Health Research Network), Portuguese Oncology Institute of Porto (IPO-Porto), Porto, Portugal
4 Comprehensive Cancer Center Raquel Seruca (Porto.CCC Raquel Seruca), 4200-072 Porto, Portugal
5 FP-I3ID, Health School of University Fernando Pessoa, Porto, Portugal

Background

Multiple myeloma (MM) is a hematologic malignancy characterized by the clonal proliferation of plasma cells, leading to the abnormal production of immunoglobulins, known as monoclonal protein (MP). Due to dysregulation of the immune system, this complex and heterogeneous disease promotes disease progression and therapeutic resistance, resulting in immunodeficiency and increased susceptibility to infections[1,2]. The identification and quantification of this pathological cell population and its corresponding MP require both serum-based (MP quantification by serum protein electrophoresis (SPE), serum free light chain ratio (rFLC) assay, and immunofixation (IF)) and cellular laboratory methods (conventional flow cytometry (FC)), which are essential for diagnosis, disease monitoring, and assessment of response to therapy[1].

Purpose

Comparative analysis of serum and cellular methods for monitoring MM.

Methods

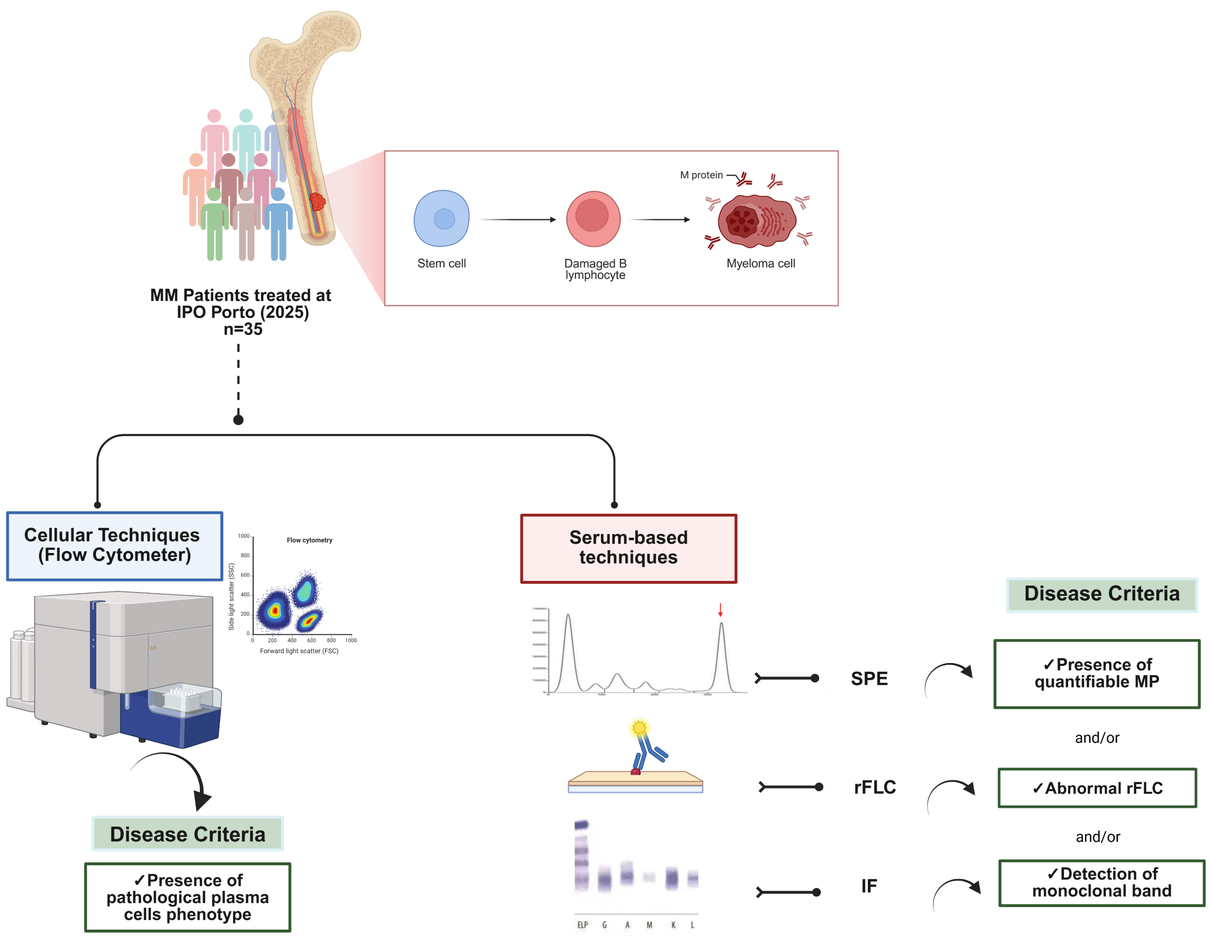

Figure 1. Laboratory strategy for cellular and serum-based disease assessment in MM.

In this study, 35 follow-up samples from patients with MM treated at our institution in 2025 were analyzed, with serum and cellular tests requested simultaneously. Laboratory evaluation included bone marrow cellular assessment by conventional FC and several serum-based techniques, including MP quantification by SPE, rFLC assay and IF. For the purposes of this comparative analysis, detectable disease was defined using simplified laboratory criteria rather than formal International Myeloma Working Group (IMWG) response criteria. In cellular analyses, disease was defined by the presence of a pathological plasma cell phenotype detected by FC. In serum analyses, disease was defined by the presence of a quantifiable MP on SPE. When the MP was not quantifiable, disease was defined by an abnormal rFLC or by the detection of a monoclonal band on IF.

Results

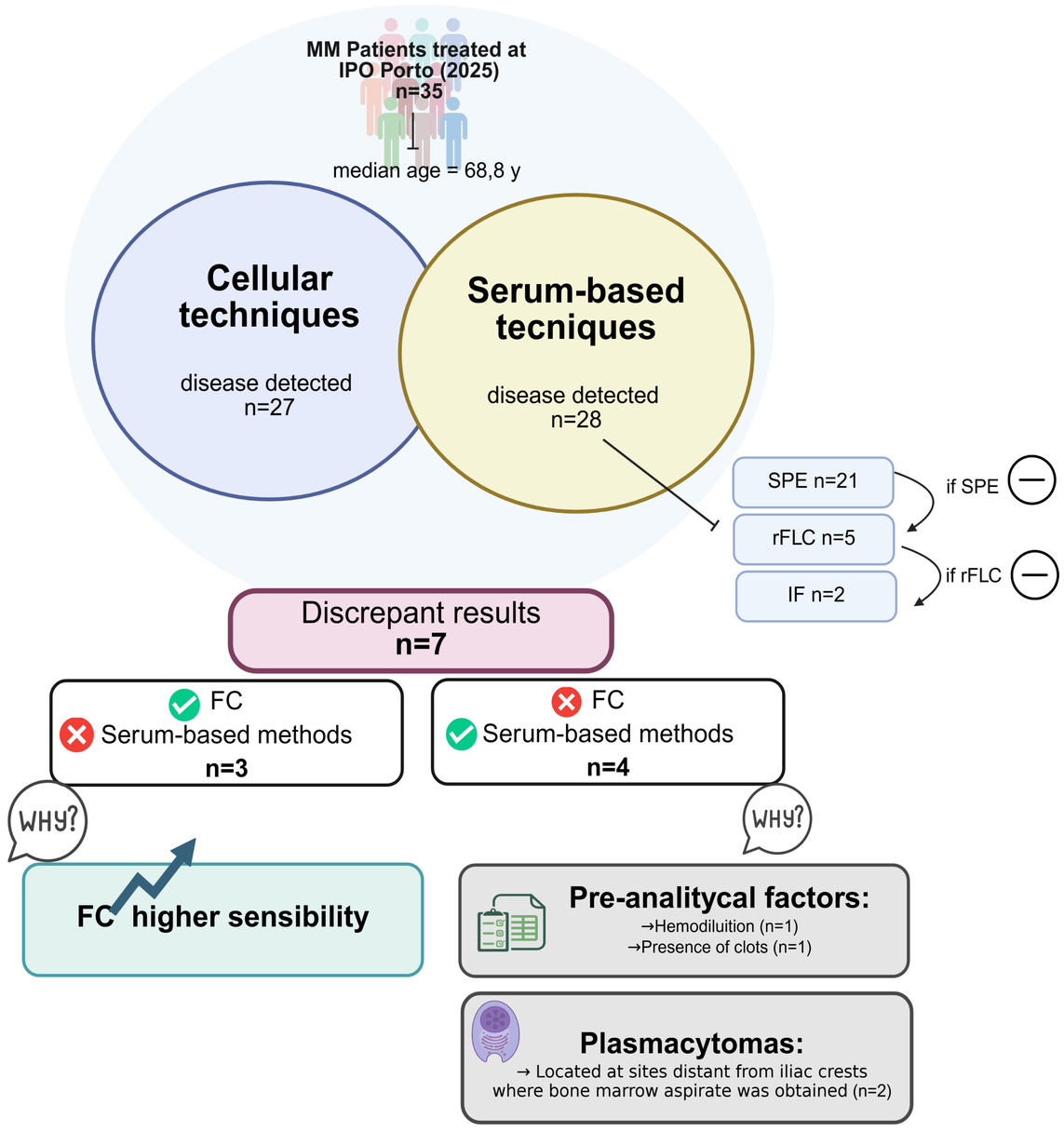

Figure 2. Comparison of FC and serum-based laboratory methods: concordance and discordance in disease detection in samples from patients with MM.

A total of 35 samples from patients previously diagnosed with MM were analyzed, with a mean age of 68.8 years. Among these 35 samples disease was detected in 27 by FC and in 28 by serum-based methods. Of the 28 samples, 21 showed a quantifiable MP on SPE and seven presented an abnormal rFLC or a monoclonal band on IF. Although the total number of samples with detectable disease was very similar between the two techniques, discrepant results were observed in seven samples. In three samples, disease was detected only by FC, whereas in the remaining four, disease was detected only by serum-based methods.

Given its higher sensitivity, FC is expected to detect disease even when serum-based methods are still negative.[3] However, it is important to examine the four cases in which disease was detected by serum-based methods but not by FC. These discrepancies were associated with pre-analytical factors (such as hemodilution or the presence of clots) or with plasmacytomas located at sites distant from the iliac crests, where the bone marrow aspirate was obtained.

Conclusion

Considering the similar detection rates obtained with both techniques, serum methods may represent a practical first-line approach for routine monitoring. Bone marrow assessment should therefore be reserved for situations in which serum-based monitoring is inconclusive or when measurable residual disease evaluation is required.

References

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