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P910 DISPARATE PREDICTION OF OUTCOMES IN A UNIFORMLY TREATED COHORT OF PATIENTS WITH AL AMYLOIDOSIS STRATIFIED BY MAYO 2012 AND EUROPEAN CARDIAC STAGING SYSTEMS

Topic: 14. Myeloma and other monoclonal gammopathies - Clinical

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Background:

Survival in systemic AL amyloidosis depends on the severity of organ involvement and haematological response to treatment. Since cardiac involvement is the major determinant of mortality, accurate staging is critical. Two validated stating systems, Mayo 2012 (stage I-IV) and European modification of Mayo 2004 (stage I-IIIb), stratify patients according to different thresholds of surrogate markers (NT-proBNP, troponin T and, for Mayo 2012, serum free light chains). However patients included in these original models were not treated with a uniform induction protocol. We report survival outcomes and impact on 6-minute walk time (6MWT) in a large cohort of uniformly treated AL amyloidosis patients stratified by both staging systems.

Aims:

We aimed to evaluate the prognostic stratification by Mayo 2012 and European staging systems in a cohort of patients treated with bortezomib-based regimens upfront and to analyse 6MWT at baseline, six and twelve months.

Methods:

Patients enrolled in a prospective observational study at the UK National Amyloidosis Centre from 2012–2017 were analysed. Patients underwent comprehensive assessments including NT-proBNP, troponin, serum free light chain and 6MWT measurement at diagnosis, 6 months and annually thereafter. Overall survival (OS) estimates were compared using Cox regression and the log-rank test.

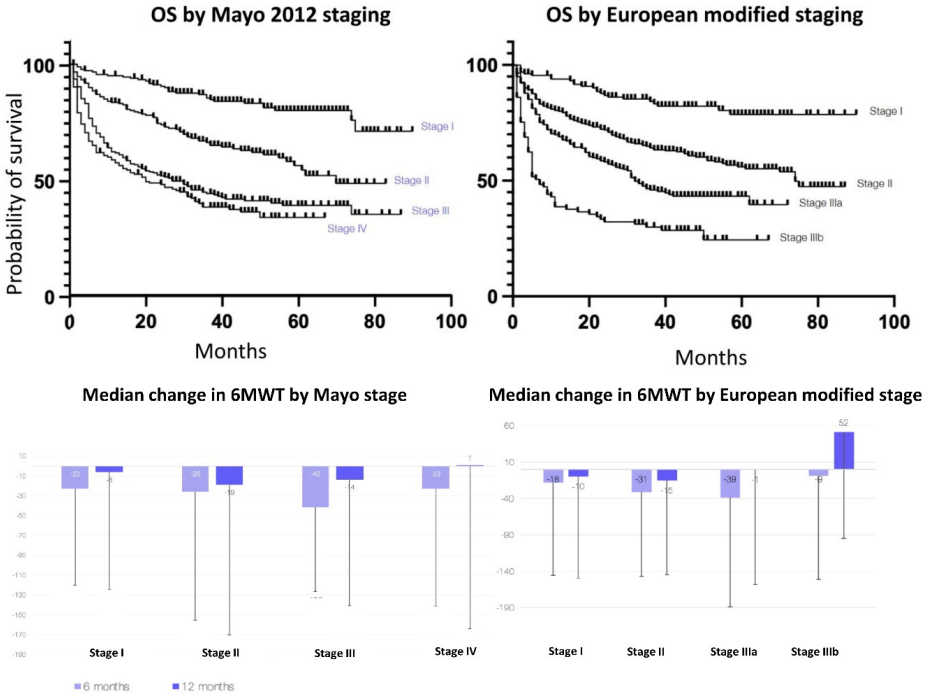
Results:

799 patients (465 male, 334 female) with a median age of 66 years (IQR 58-72) were included. The median OS was 74 months (95% CI 68-79). There was no significant difference in OS for Mayo 2012 stage III vs IV patients (median 27 vs 20 months, p=0.18) but was a difference in stage IIIa vs IIIb (32 vs 7 months, p<0.0001). Median baseline 6-minute walk distance was 362m (IQR 230-460) and significantly decreased with worsening cardiac stage across both staging systems at all time points (p<0.0001). After 6 months, median 6MWT had decreased by a median of 28m across all Mayo stages and all haematological responses (CR, VGPR, PR, NR). After 12 months, 6MWT improved most significantly by median 8m and 81m in Mayo IV and European modified IIIb patients in CR but not for any other haematologic response category (<VGPR). However, using the European modification cardiac stage, there was no improvement in for patients with stage IIIa disease (median -1m) whilst there was marked improvement (median 52m) for stage IIIb patients at 12 months over baseline.

On multivariable analysis, an improvement by >44m from baseline at 6 months (Mayo: HR 0.58 p=0.033; European: HR 0.57, p=0.0435) or 12 months (Mayo: HR 0.58 95% p=0.018; European: HR 0.6253, p=0.0467) was an independent predictor of better outcomes in a model that included haematological responses and (separately) Mayo 2012/European modified staging systems independently.

Summary/Conclusion:

6MWT worsens with increasing cardiac disease stage. Whilst improvement is an independent prediction of better survival, marked improvements are mainly seen in patients with advanced stage disease. These improvements differ significantly depending on the cardiac staging system (stage III/IV Mayo 2012; whilst only in stage IIIb in European modified staging). In a uniformly treated cohort, Mayo 2012 staging does not stratify patients adequately for advanced disease. These finding suggest the need to harmonise cardiac staging systems and will have a serious impact on the use of 6MWT as a clinical trial end point.



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