

Comorbidity indices for prognostic evaluation in multiple myeloma: a comprehensive evaluation of the Revised Myeloma Comorbidity Index and other comorbidity indices with pro- and retrospective applications

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Supplementary Table 1.

Overview of assessed comorbidity indices, including their risks and classification into risk groups

| Comorbidity score | Revised Myeloma Comorbidity Index (R-MCI) (weight points) | International Myeloma Working Group (IMWG)-frailty index (weight points) | Charlson Comorbidity Index (CCI) (weight points) | Mayo risk score (weight points) | UK Myeloma Research Alliance Risk Profile (MRP) |
|---|--|--|---|------------------------------------|---|
| Risk factors and weighting | moderate/severe lung disease ¹ (1) | CCI ≥2 (1) | chronic lung disease (1) | Age ≥70 yrs (1) | Age |
| | eGFR <60 ² (1) | Age 76-80 yrs (1) Age >80 yrs (2) | moderate/severe kidney disease (2) | ECOG-PS ≥2 (1) | ECOG-PS |
| | KPS 80-90% (2) KPS ≤70% (3) | IADL ≤6 (1) | myocardial infarction (1) congestive heart failure (1) | Pro-BNP ≥300 ⁶ (1) | ISS |
| | Age 60-69 yrs (1) Age ≥70 yrs (2) | ADL ≤4 (1) | peripheral vascular disease (1) | | CRP ⁷ |
| | moderate/severe frailty ³ (1) | | cerebrovascular disease/accident (1) dementia (1) | | |
| +/- unfavorable cytogenetics ⁴ (1) | | liver disease mild (1) or moderate/severe (3) | | | |
| | | solid tumor (2) metastatic solid tumor (6) leukemia (2) lymphoma ⁵ (2) | | | |
| | | diabetes mellitus Ø end-organ damage (1) with end-organ damage (2) | | | |
| | | connective tissue disease (1) | | | |
| | | AIDS (6) ulcer (1) hemiplegia (2) | | | |
| Fit | 0 to 3 points ⁸ | 0 points ⁸ | <2 points ⁸ | 0 points ⁸ | |
| Intermediate-fit | 4 to 6 points ⁹ | 1 point ⁹ | | 1 to 2 points ⁹ | |
| Frail | 7 to 9 points ¹⁰ | ≥2 points ¹⁰ | ≥2 points ¹⁰ | 3 points ¹⁰ | |
| Reference | Engelhardt 2017 | Palumbo 2015 | Charlson 1987 | Milani 2016 | Cook 2019 |

Definitions and abbreviations:

¹moderate lung disease = FEV₁ 50-80%, severe lung disease = FEV₁ <50%, ²in ml/min/1.73m², ³defined by Fried et al. 2001 and Woo et al. 2012, ⁴defined as t(4;14), t(14;16), t(14;20), del(17p), del(13q14), hypodiploidy, c-myc, chromosom-1-aberrations, yrs: years

⁵For calculation of the CCI, the diagnosis Multiple Myeloma was not included, ⁶ng/L, ⁷mg/dl,

⁸definition of low-risk or fit patients, ⁹intermediate-risk or intermediate-fit patients, ¹⁰high-risk or frail patients

Number in brackets: weights of respective risk factor

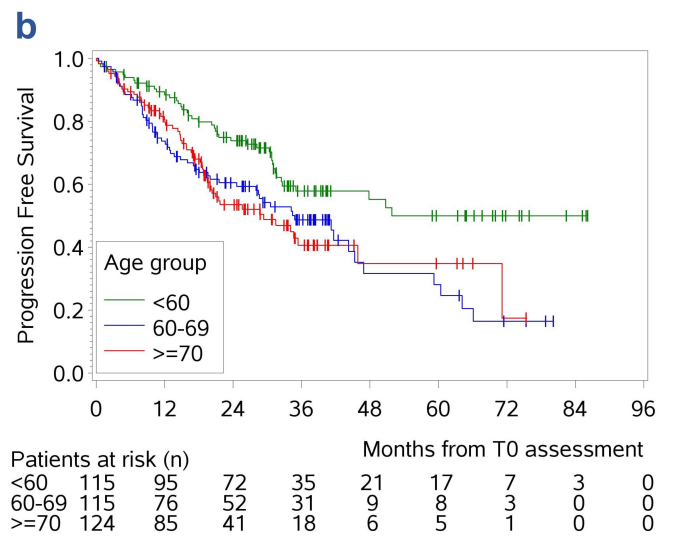
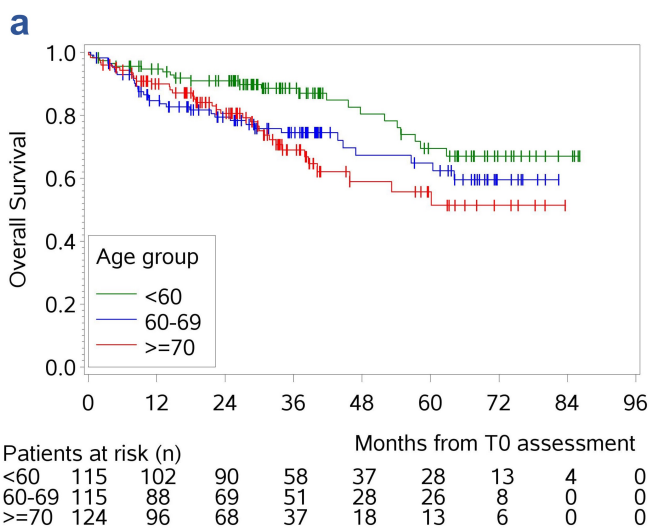
Supplementary Table 2.

Overview of 5 comorbidity indices including their risks, risk group distribution via retrospective and prospective analyses, 3-year-OS and PFS group separations with respective scores using our prospective data, and advantages and challenges of each score

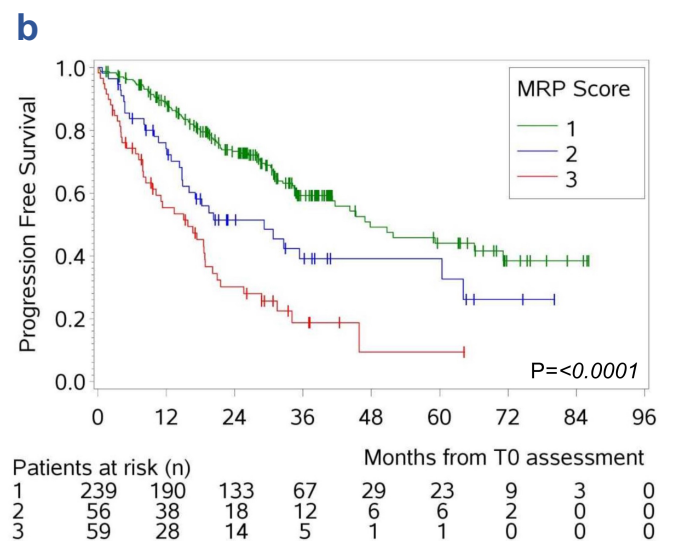
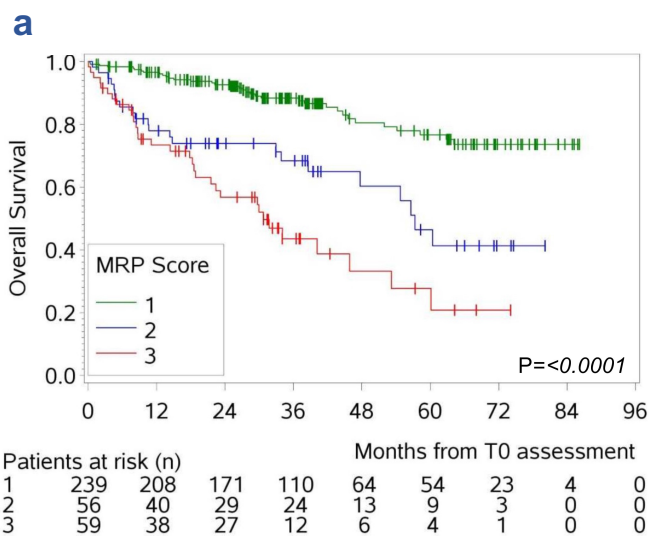
| | Revised Myeloma Comorbidity Index (R-MCI) | | International Myeloma Working Group (IMWG)-frailty index | | Charlson Comorbidity Index (CCI) | | Mayo risk score | | UK Myeloma Research Alliance Risk Profile (MRP) |
|------------------------------------|--|--------------|--|--------------|---|--------------|--|--------------|---|
| Risk parameters used | eGFR Lung function KPS Frailty Age +/- Cytogenetics | | ADL IADL CCI Age | | 19 differently weighted categories Age included | | ECOG-PS NT-proBNP Age | | ECOG-PS ISS CRP Age |
| Reference | Engelhardt et al., Haematologica 2017 | | Palumbo et al., Blood 2015 | | Charlson et al., 1987, J. Chronic Dis | | Milani et al., Am J Hematol. 2016 | | Cook et al., Lancet Haematol.2019 |
| Risk group distribution (%) | Retro-spective | Pro-spective | Retro-spective | Pro-spective | Retro-spective | Pro-spective | Retro-spective | Pro-spective | Excluded due to missing laboratory data |
| Low-risk | 27% | 26% | 41% | 30% | 65% | 47% | 29% | 37% | |
| Intermediate-risk | 55% | 60% | 22% | 36% | - | - | 58% | 55% | |
| High-risk | 18% | 14% | 37% | 34% | 35% | 53% | 13% | 8% | |
| p-value | 0.2633 | | <0.001 | | <0.001 | | 0.0150 | | |
| 3-yr-OS | 91% | | 95% | | 91% | | 93% | | 88% |
| Low-risk | 77% | | 82% | | - | | 72% | | 68% |
| Intermediate-risk | 52% | | 60% | | 67% | | 29% | | 44% |
| High-risk | <0.0001 | | <0.0001 | | <0.0001 | | <0.0001 | | <0.0001 |
| p-value | <0.0001 | | <0.0001 | | <0.0001 | | <0.0001 | | <0.0001 |
| 3-yr-PFS | 70% | | 74% | | 61% | | 63% | | 59% |
| Low-risk | 45% | | 44% | | - | | 44% | | 39% |
| Intermediate-risk | 28% | | 35% | | 40% | | 0% | | 19% |
| High-risk | <0.0001 | | <0.0001 | | 0.0005 | | <0.0001 | | <0.0001 |
| p-value | <0.0001 | | <0.0001 | | 0.0005 | | <0.0001 | | <0.0001 |
| Advantage | Time effective (user-friendly homepage) Pro- and retrospectively assessable | | Internationally tested User-friendly homepage | | Long known and used | | Time-effective | | Significant risk group distribution in prospective assessment |
| Challenge | Less international use yet; All 5 risk scores lesser used than desired by MM experts* | | Not retrospectively assessable No clear distinction between low- and intermediate-groups using prospective data | | Not MM specific Time consuming to assess More favorable results in retrospective assessment | | NT-pro BNP not routinely assessed → impossible to assess if NT-pro BNP is missing | | |

Abbreviations:

eGFR: estimated glomerular filtration rate; KPS: Karnofsky performance status, ADL: activity of daily living, IADL: instrumental activity of daily living; ECOG-PS: ECOG performance status, ISS: international staging system, CRP: C-reactive protein; yr: year; OS: overall survival, PFS: progression free survival; * personal communication Evangelos Terpos, Athens, Greece, educational EHA meeting, Vienna, 2022: "25% of the MM experts and physicians use frailty risk scores to aid in risk assessment and clinical decision making, but 75% do not and rather rely on their clinical judgement alone".



Suppl. Figure 1



Suppl. Figure 2

Supplementary Figures

Supplementary Figure 1. Kaplan-Meier estimates for overall- and progression-free survival (prospective cohort / n=354) in different age groups

- (a) OS and
- (b) PFS for three different age groups (<60 years vs. 60-69 years vs. ≥70 years)

Abbreviations: OS: Overall Survival; PFS: Progression Free Survival

Supplementary Figure 2. Kaplan-Meier estimates for overall- and progression-free survival (prospective cohort / n=354) according to different comorbidity scores in prospective cohort

- (a) OS and
- (b) PFS for MRP-Score

Abbreviations: OS: Overall Survival; PFS: Progression Free Survival; MRP Score: UK Myeloma Research Alliance Risk Profile Score