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## Diagnostic Timing And Slim-Crab Presentations In Multiple Myeloma: A Real-World Healthtree Cure Hub Registry Study (2006–2024)

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### Background

The 2014 revision of the International Myeloma Working Group (IMWG) diagnostic criteria for multiple myeloma (MM) introduced the SLiM biomarkers—≥60% bone marrow plasma cells, abnormal serum free light chain ratio ≥100, and more than one focal lesion on MRI—to enable earlier diagnosis and treatment before end-organ damage. While this conceptual shift marked a milestone in the evolution of MM care, its real-world effect on diagnostic timing remains poorly characterized.

### Purpose

To analyze the time from the first SLiM-CRAB feature appearance to MM diagnosis and explore how presentation patterns evolved over the years.

### Methods

We analyzed 584 patients from the HealthTree Cure Hub Registry diagnosed with MM between 2006 and 2024. Patients were included if structured and unstructured electronic health record (EHR) data were available to determine SLiM and CRAB status at diagnosis. RSLiM-CRAB features were derived from structured EHR inputs and laboratory values. Bone marrow plasma cell percentage, serum free light chain (FLC) ratio, renal function (creatinine), calcium, hemoglobin, and skeletal involvement were assessed. Notably, radiographic bone involvement and MRI data—frequently embedded in unstructured reports—were extracted using a GPT-o1-based few-shot prompting model, which had been internally validated against manual abstraction with a classification accuracy of 98%. Patients were stratified into three diagnostic subgroups: SLiM-only, CRAB-only, and SLiM+CRAB, reflecting their presenting clinical phenotype.

The primary outcome was the diagnostic interval, defined as the number of days between the first SLiM or CRAB feature and the date of MM diagnosis (EOD-MM). Summary statistics (medians, interquartile ranges) were calculated for each group. Linear regression was used to evaluate the association between diagnosis year and EOD-MM, adjusting for SLiM-CRAB group. Additional regression models compared EOD-MM across diagnostic subgroups using SLiM-only group as the reference category.

### Results

At diagnosis: 26.7% were SLiM-only, 33.6% CRAB-only, and 39.7% SLiM+CRAB. SLiM+CRAB presentations rose from 23.5% (2014) to 44.4% (2024). Median intervals were 25 days (Q1-Q3 = 8.5-65) before and 31 days (Q1-Q3 = 14-83.8) after 2014 ( $p=0.64$ ). Diagnosis year was not a significant predictor of EOD-MM. Compared to SLiM-only, CRAB-only ( $\beta = -229.5$ ,  $p<0.001$ ) and SLiM+CRAB ( $\beta = -157.0$ ,  $p<0.001$ ) showed shorter EOD-MM. Table 1 summarizes feature prevalence and associations of EOD-MM by diagnosis year.

**Table 1. Time from SLiM-CRAB Onset to Multiple Myeloma Diagnosis**

Year	N	Median (days)	IQR (days)	Q1 (days)	Q3 (days)	Mean (95% CI)	SLiM only	CRAB only	SLiM + CRAB	Coef (p-value)
All	556	31	69.5	13.75	83.25	131.4 (102.7–160.1)	144 (25.9%)	180 (32.4%)	232 (41.7%)	—
2006 - 2014	34	25.5	56.5	8.5	65	134.6 (43.8–225.5)	15 (44.1%)	10 (29.4%)	9 (26.5%)	Ref ***
2015	17	23	36	7	43	73.3 (6.3–140.3)	5 (29.4%)	4 (23.5%)	8 (47.1%)	-42.5 (p=0.671)
2016	19	43	43.5	15.5	59	127.8 (20.1–235.5)	7 (36.8%)	5 (26.3%)	7 (36.8%)	2.3 (p=0.981)
2017	31	40	68	21.5	89.5	124.0 (27.1–220.9)	12 (38.7%)	4 (12.9%)	15 (48.4%)	-14.1 (p=0.866)
2018	52	24.5	50.5	10.5	61	164.2 (36.0–292.5)	16 (30.8%)	18 (34.6%)	18 (34.6%)	54.3 (p=0.465)
2019	71	31	49.5	17	66.5	129.0 (56.6–201.4)	20 (28.2%)	19 (26.8%)	32 (45.1%)	17.5 (p=0.804)
2020	75	30	43.5	14.5	58	161.0 (34.6–287.5)	21 (28.0%)	26 (34.7%)	28 (37.3%)	55.5 (p=0.427)
2021	96	32	68.5	13	81.5	157.0 (83.9–230.0)	17 (17.7%)	40 (41.7%)	39 (40.6%)	72.7 (p=0.284)
2022	60	31	71.75	12.75	84.5	91.1 (49.8–132.4)	10 (16.7%)	22 (36.7%)	28 (46.7%)	4.8 (p=0.947)
2023	75	38	88	13.5	101.5	113.1 (62.5–163.8)	16 (21.3%)	23 (30.7%)	36 (48.0%)	15.2 (p=0.829)
2024	26	32	116.75	11.25	128	84.1 (32.4–135.8)	5 (19.2%)	9 (34.6%)	12 (46.2%)	-7.7 (p=0.931)

\*\*\*SLiM-Only Group was used for Reference: With CRAB-Only Coef = -229.507 ( $p<0.001$ ) and SLiM+CRAB Coef = -157.049 ( $p<0.001$ ).

SLiM and CRAB groups reflect diagnostic feature presence at MM diagnosis. Values are presented as counts with percentages. Time from SLiM-CRAB onset to multiple myeloma diagnosis values shown are median, first and third Quartile (Q1 and Q3). Mean values reported with 95% confidence intervals. Years 2006–2014 were grouped due to small sample size. Regression  $\beta$  coefficients (coef) and p-values were reported for the linear regression of time from SLiM-CRAB onset to MM diagnosis on year (reference =  $\leq 2014$ ), adjusting for SLiM-CRAB group.

### Conclusion

In this cohort, 2006-2024 EOD-MM remained stable, with no significant difference before/after 2014. However, CRAB only and SLiM+CRAB group were significantly negatively associated with EOD-MM, highlighting challenges in identifying MM in the absence of CRAB. The spike in SLiM-only cases after 2014 may reflect both increased clinical awareness and retrospective reclassification of patients previously labeled as smoldering. Study limitations include potential under documentation and study of SLiM features in earlier years, exclusion of patients with incomplete diagnostic timelines, and SLiM-CRAB underreporting prior to widespread EHR adoption.