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Unraveling the Dynamics of Protein Secretion in Multiple Myeloma: A Comparative Study of Non-Secretory Patterns and Disease Evolution

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BACKGROUND

Non-secretory multiple myeloma (NSMM), 1-2% of all multiple myeloma (MM) cases, was traditionally defined by the absence of detectable M-Spike in serum or urine. Advancements in diagnostic methodologies have revealed that a proportion are more accurately categorized as oligo-secretory. Disease evolution significantly impacts monitoring, progression, and prognosis. This study examines MM secretion patterns (SP) and evolution by comparing current classification with medical notes.

METHODOLOGY

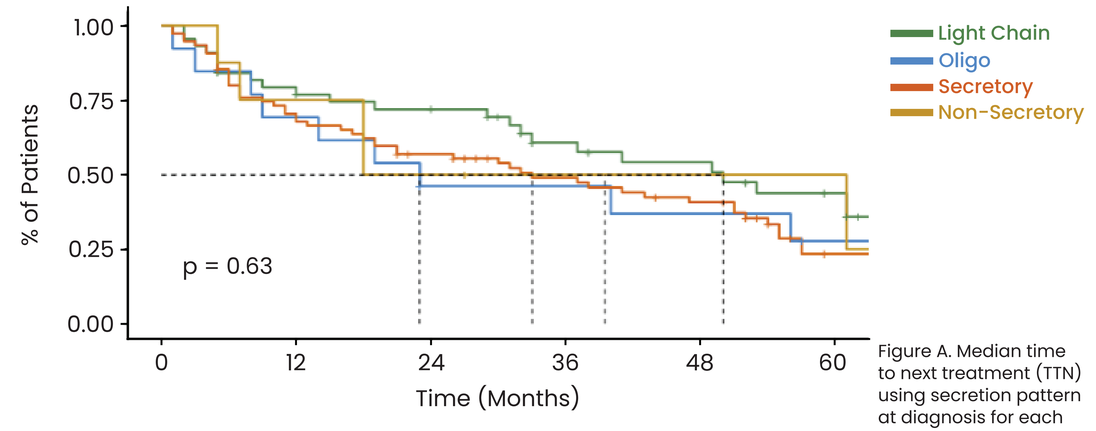
Using HealthTree Cure Hub, we analyzed real-world data from 140 patients. SP evolution was assessed as Secretory (SC), Light Chain Only Oligosecretory (LCO), Heavy Chain Oligosecretory (HCO), and True Non-secretory (TNSC) at diagnosis and last lab follow-up. TNSC patients showed no myeloma activity on the M-protein, and light chain assay. LCO patients exhibited activity only on their light chain assay. HCO patients met the IMWG criteria for Non-Measurable Myeloma. SC patients didn't meet the criteria for the other categories. Changes to less secretory patterns were recorded based on office notes, indicating a relapse diagnosis.

RESULTS

Patients were 65±8.5 yr, and 56.5% were female. Of the 122 patients with mSMART stage available, 13% were high-risk, and 6% were double-hit. At their last follow-up, the SPs of the 140 patients analyzed were as follows: 48% SC, 28.5% LCO, 10% HCO, and 13.5% TNSC patients. When comparing SPs at the time of MM diagnosis, 16 patients (11.5%) were found to have changed to a less secretory type. This change took a mean of 66.5 months from the time of diagnosis, with SC-to-HCO (43.25 mo) and HCO-to-TNSC (34.5 mo) being the fastest and SC-to-TNSC being the slowest (96.5 mo). Among the 73 patients with LCO, HCO, or TNSC patterns, 75.3% had their SP accurately reported, 12.3% had it incorrectly classified, and 12.3% were not classified. The median TTNTs of the observed events at last fo llow-up using the SP at diagnosis were: SC (39 mo), LCO (50 mo), HCO (23 mo), and TNSC (33 mo) (p = 0.63). The median TTNTs, when using the current SP, were: SC (32 mo), LCO (50 mo), HCO (31.5 mo), and TNSC (33 mo) (p = 0.44). After two years of follow-up, the TTNT survival rates using the SP at diagnosis were: SC (53.3%), LCO (65.9%), HCO (38.5%), and TNSC (50%). The TTNT survival rates, when using the current SP, were: SC (50.7%), LCO (67.5%), HCO (42.9%), and TNSC (57.9%).

CONCLUSION

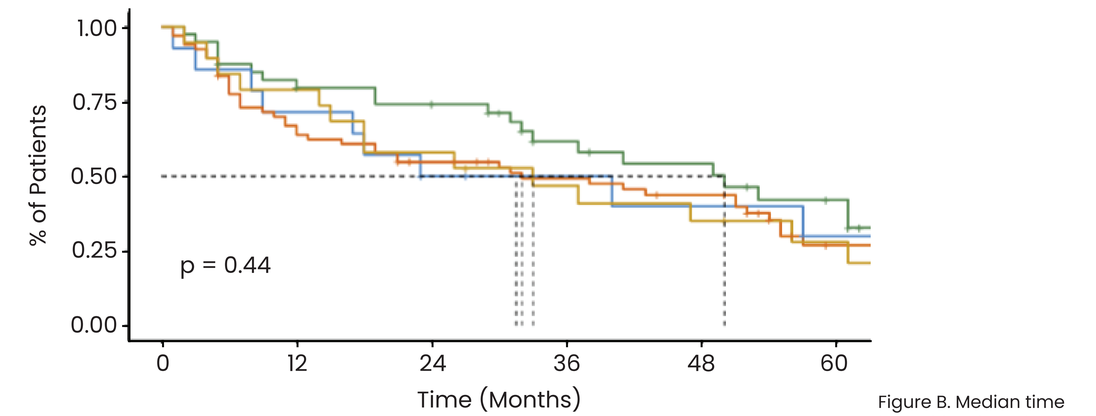
Our study elucidates the dynamic evolution of MM SPs, with 11.5% of patients transitioning to less secretory types. The study findings suggests that the NSMM at onset does not confer additional risk. Interestingly, we found no retrospective impact of SP evolution at disease onset, which has been linked to a worse prognosis at relapse. However, one of four patients had inaccurate or missing SP information in their office notes, highlighting the need for improved documentation and awareness.



Light Chain	44	33	29	19	16	11
Oligo	13	9	4	5	4	2
Secretory	75	52	40	30	24	8
Non-Secretory	8	6	4	3	3	2

Figure A. Median time to next treatment (TTN) using secretion pattern at diagnosis for each group.

Light Chain=Light Chain Only Oligosecretory, Oligo=Heavy Chain Oligosecretory, Non-Secretory=True Non-Secretory.



Light Chain	40	31	27	17	14	9
Oligo	14	10	6	5	4	2
Secretory	67	44	34	27	23	8
Non-Secretory	19	15	11	8	6	4

Figure B. Median time to next treatment (TTN) for current secretion patterns by group.

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