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POSTER ABSTRACTS

654.MGUS, AMYLOIDOSIS AND OTHER NON-MYELOMA PLASMA CELL DYSCRASIAS: CLINICAL AND EPIDEMIOLOGICAL

Sars-Cov-2 Infection Does Not Lead to Progression of Monoclonal Gammopathy of Undetermined Significance: Results from the Population-Based Istopmm Screening Study

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Background

The mechanisms that lead to the progression from monoclonal gammopathy of undetermined significance (MGUS) to multiple myeloma (MM) and related disorders are largely unclear. Infections have been hypothesized to play a role in the onset of MM through dysregulation of the immune response or chronic immune stimulation. Therefore, the effect of concurrent viral infection, for example SARS-CoV-2 infection, might increase the risk of MGUS progression to MM.

In Iceland, widespread and easy access to PCR testing for SARS-CoV-2 was implemented early in the COVID-19 pandemic, leading to very high testing rates. This provides a unique opportunity to evaluate whether PCR-proven SARS-CoV-2 infection has an impact on the risk of MGUS progression. To study this relationship, we performed a prospective nationwide study based on data from the Iceland Screens, Treats, or Prevents Multiple Myeloma (iStopMM) study.

Methods

A total of 75,422 individuals were screened for M protein and free light chains (FLC) between September 2016 and December 2020, and 3,358 individuals were diagnosed with MGUS and randomized to one of three study arms, two of which (n=2,037) are followed longitudinally with repeated serum protein electrophoresis (SPEP) and FLC analysis. These two arms comprised the study population.

Iceland enforced a strict COVID-19 screening policy at the beginning of the pandemic where individuals suspected of having SARS-CoV-2 infection, exposed to SARS-CoV-2, or as part of a screening program underwent PCR testing. This screening policy ended on February 23 rd, 2022. All PCR test results in Iceland (positive or negative) and SARS-CoV-2 vaccinations were centrally registered, providing complete nationwide information on SARS-CoV-2 infections and vaccination coverage. By cross linking this data to the iStopMM database, individuals with MGUS who underwent PCR testing for SARS-CoV-2 in Iceland were identified.

As M protein levels change over time, a linear mixed model with random intercept and slope was used to estimate changes in M protein concentration as a function of age, before and after SARS-CoV-2 infection. The slope of the evolution of M protein

level over age was modelled using a restricted cubic spline to determine the effects of a proven infection on changes in M protein levels.

Results

A total of 1,305 individuals (53% males) with MGUS who had undergone at least one PCR test for SARS-CoV-2 were identified. Median age was 66 years (range: 41-97) and median M protein concentration at study inclusion was 2.0 g/L (range: 0-26.0). 5,401 PCR tests were performed in this group, with a median of two PCR tests (range: 1-68) per individual. 188 individuals tested positive for SARS-CoV-2 (14.4%), and 19 individuals (10.1%) had not received SARS-CoV-2 vaccination at the time of infection. In all, 5,473 serum samples were analyzed for M protein concentration, of which 347 (6.4%) were obtained a median 107 days (interquartile range: 45-213) after a confirmed SARS-CoV-2 infection (Table 1).

After adjusting for age, sex, calendar year, and SARS-CoV-2 vaccination status, no difference in M protein concentration was observed when comparing samples obtained before or after a positive test result (exponentiated beta coefficient (Exp(β)): 1.01; 95% confidence interval [CI], 0.91-1.12). The same was true when analyzed for each sex separately (Figure A). Analysis of the effect of SARS-CoV-2 infection on M protein development in a subset of unvaccinated individuals (n=19) demonstrated a 40% increase in M protein concentration following SARS-CoV-2 infection when compared to those who were vaccinated at time of infection (Exp(β): 1.4; 95% CI, 1.1-1.8).

Summary

In this large population-based screening study that included 1,305 individuals with MGUS who had undergone PCR testing and were observed before and after SARS-CoV-2 infection, we found no evidence of SARS-CoV-2 infection being associated with progression from MGUS to MM. A small subset of unvaccinated individuals had a significant increase in M protein concentration after SARS-CoV-2 infection compared to vaccinated individuals who were infected. Compared to the remainder of the iStopMM cohort, the subset of unvaccinated individuals had higher M protein concentration at baseline which implied a higher baseline risk of progression. Overall, our study shows that infection with SARS-CoV-2 is not associated with an increased risk of progression from MGUS to MM.

Disclosures Hultcrantz: *Amgen, Daiichi Sankyo, GlaxoSmithKline:* Research Funding; *Curio Science LLC, Intellisphere, Bristol Myer Squibb, GlaxoSmithKline:* Honoraria. **Harding:** *Bindingsite ltd.:* Current Employment, Membership on an entity's Board of Directors or advisory committees. **Landgren:** *Merck:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Other: Membership on independent data monitoring committees; *Amgen:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Other: Membership on independent data monitoring committees; *Takeda:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Other: Membership on independent data monitoring committees; *Janssen:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Other: Membership on independent data monitoring committees; *Celgene:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Other: Membership on independent data monitoring committees; *Adaptive:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Other: Membership on independent data monitoring committees; *Theradex:* Consultancy, Honoraria, Membership on an entity's Board of Directors or advisory committees, Other: Membership on independent data monitoring committees. **Kristinsson:** *Celgene:* Research Funding; *Amgen:* Research Funding.

Table 1. Exponentiated beta coefficients with 95% confidence interval (CI) from mixed linear models of the log M protein concentration (g/L), with random intercept and slope. All estimates are adjusted for age, sex, and calendar year.

	Number of samples		Median M-protein concentration g/L		Exp(beta) (95% CI) After Covid-19 vs. Without/before Covid-19	P-value interaction
	After Covid-19	Without/before Covid-19	After Covid-19	Without/before Covid-19		
Overall	347	5,126	1.8	1.3	1.01 (0.91, 1.12)	
Sex						
Males	239	2,680	1.6	1.5	1.0 (0.8, 1.1)	0.11
Females	108	2,446	3.4	1.1	1.1 (1.0, 1.3)	
Age						
≤60 years	91	1,192	1.0	1.2	0.8 (0.7, 1.0)	<0.01
61-80 years	215	3,302	2.2	1.3	1.1 (1.0, 1.3)	
>80 years	41	632	1.4	1.4	0.8 (0.6, 1.0)	
Vaccinated						
No	54	3,974	7.4	1.3	1.4 (1.1, 1.8)	<0.01
Yes	293	1,152	1.6	1.3	1.0 (0.9, 1.1)	
Number of doses						
1	31	228	0.7	1.2	1.2 (0.8, 1.7)	<0.01
2	175	831	2.3	1.2	1.1 (1.0, 1.3)	
3	87	93	1.3	3.1	0.7 (0.5, 0.9)	

Figure A. Predicted levels of the M protein concentration (g/L) with 95% confidence intervals (shaded area) at different ages without or before a positive PCR test for SARS-CoV-2, by sex.

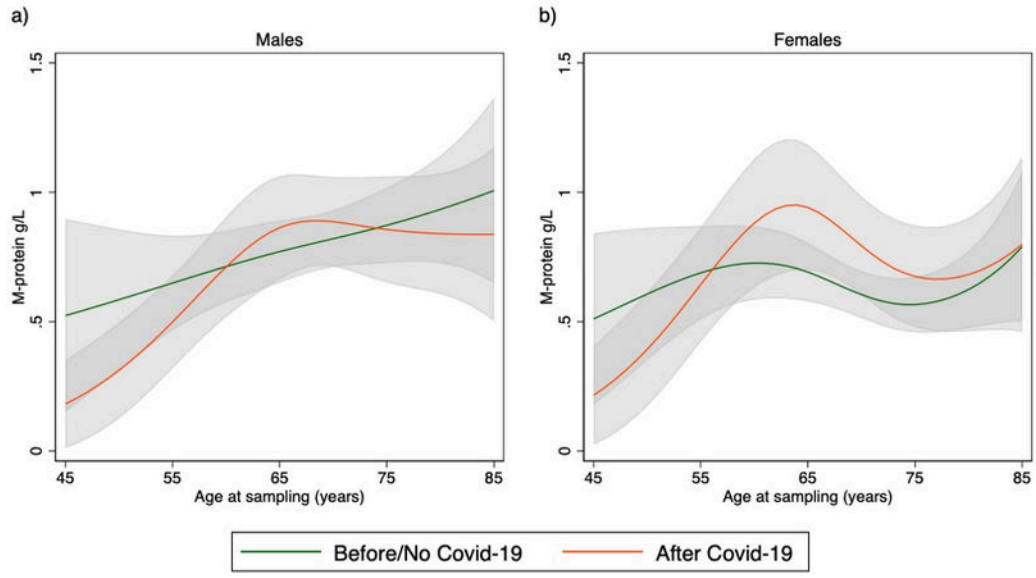

Figure 1

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