Does familial disease impact prognosis and treatment outcome in WM?

Sigurdur Kristinsson

Relatives of patients with lymphoplasmacytic lymphoma/Waldenström's macroglobulinemia have increased risk of lymphoproliferative disorders, and an earlier single-center study found conflicting results regarding prognosis in familial Waldenström's macroglobulinemia. We conducted a nationwide study to determine the impact of familial lymphoplasmacytic lymphoma/Waldenström's macroglobulinemia on overall survival. Through nationwide Swedish registries and a national hematology/oncology network we identified 2,185 lymphoplasmacytic lymphoma/Waldenström's macroglobulinemia patients and their 6,460 first-degree relatives. Family history of any lymphoproliferative disorder was defined as having a first-degree relative with lymphoplasmacytic lymphoma/Waldenström's macroglobulinemia, Hodgkin lymphoma, non-Hodgkin lymphoma, multiple myeloma, chronic lymphocytic leukemia and/or monoclonal gammopathy of undetermined significance. Cox proportional hazard model was used for statistical analysis to obtain hazard ratios and 95% confidence intervals. Family history of any lympho-proliferative disorder (compared to sporadic form) was significantly associated with increased risk of death (hazard ratio 1.34; 95% confidence interval 1.03-1.75) and increasing number of relatives diagnosed with a lympho-proliferative disorder was associated with higher risk (1.22; 0.99-1.50), although borderline significant. In this nationwide study we thus found that familial lympho-plasmacytic lymphoma/Waldenström's macroglobulinemia has worse overall survival (compared to sporadic). Our findings together with published papers suggest that familial lymphoplasmacytic lymphoma/Waldenström's macroglobulinemia may have a different biology, prognosis and response to therapy.

Table.1

Risk of death in LPL/WM patients in relation to family history of lymphoproliferative disorders

	No. of patients	HR*	95% CI
Family history of:			
Any lymphoproliferative disorder	93	1.34	1.03-1.75
Per increasing number of relatives**		1.22	0.99-1.50
Multiple myeloma	13	1.47	0.76-2.85
Non-Hodgkin lymphoma* **	44	1.43	1.00-2.06
Hodgkin lymphoma	4	0.51	0.13-2.03
Chronic lymphocytic leukemia	17	1.43	0.71-2.88
Lymphoplasmacytic lymphoma/Waldenström's macroglobulinemia	16	1.28	0.69-2.39
Monoclonal gammopathy of undetermined significance	11	1.12	0.53-2.37
Any lymphoproliferative disorder (Age-scale)		1.32	1.02-172
Any lymphoproliferative disorder (Year of diagnosis-scale)		1.31	1.01-1.71
Age at diagnosis (per one year increase)		1.06	1.05-1.07
Female gender		0.72	0.65-0.79
Year of diagnosis (per one year increase)		0.99	0.98-1.00

*Cox model adjusted for age at diagnosis, gender and year of diagnosis.
**The additive risk of each first-degree family member diagnosed with an LP.
***Family members with non-Hodgkin lymphoma, excluding those with LPL/WM