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Comorbidity, age and sex in relation to survival among 2264 patients with Waldenstrom's macroglobulinemia – a Swedish Lymphoma Registry Study

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Waldenstroms macroglobulinemia (WM) is a rare indolent B-cells lymphoma mainly affecting elderly persons. High age is a strong negative prognostic factor as with increasing age many patients develop comorbidities, influencing both the choice of treatment and mortality.

The aim with this study is to analyse clinical characteristics, sex, comorbidity and mortality, with the intent to improve treatment decisions in both male and female WM patients, especially in the elderly.

Methods

All patients with a diagnosis of WM or lymphoplasmacytic lymphoma (n=2264) registered in the Swedish Lymphoma Registry (SLR) and matched controls (n=22595) between 1 January 2000 to 31 December 2019 were included. Information on comorbidities within 10 years prior to diagnosis of WM were obtained from the Swedish Patient Register and classified according to the modified Charlson comorbidity index (CCI): CCI 0 (no comorbidity) CCI 1 (mild comorbidity), or CCI 2+ (severe comorbidity). The date and the main cause of death was obtained from the Swedish Cause of Death Register.

Results

From SLR we identified 2 264 patients with WM, 1378 (61%) males and 886 (39%) females. The median age at diagnosis was 73 years.

The difference in prediagnostic comorbidity using CCI showed that WM patients had a worse CCI than the controls; CCI 0 in 1187/2264 (52.4%) and 12573/22595 (55.6%), respectively (P-value < 0.001). WM patients had significant more often rheumatic, renal, severe liver diseases, and other malignancies, but significantly less often myocardial infarction, cerebrovascular diseases or dementia compared with the controls.

CCI was increasing with age, CCI 0 and CCI ≥ 2 for patients ≤65 years were 441/568 (72.4%) and 98/568 (17.3%), the corresponding figures for patients ≥76 years were 379/958 (39.6 %) and 404/958 (42.2%), respectively.

Male WM patients had CCI ≥2 in 471/1378 (34.3%) and females 269/891 (29.9%). The difference was even more pronounced in the oldest cohort (≥76 years); 266/575 (46.3%) and 138/383 (36.0%), respectively. The comorbidity differed between the sexes, male WM patients had more cardiovascular diseases, congestive heart failure, peripheral vascular and renal diseases and female WM patients had more rheumatic diseases.

Lymphoma was the cause of death in 449/1104 (40.7%) of the WM patients. In the oldest cohort (≥76 years) even less patients (229/635 or 36.1%) died of lymphoma. The most common non-lymphoma deaths were due to cardiovascular disease (17.0%) and cancer (13.5%). Fig 1 and 2.

Patients with CCI 1 and CCI ≥2 had both a higher non-lymphoma mortality and lymphoma-specific mortality than patients without comorbidities at diagnosis. The risk factors for lymphoma-specific mortality were high age and early year of diagnosis, PS 1-4, high comorbidity (CCI ≥2) and male sex.

There was no significant difference in OS between different first-line treatments (DRC, R-bendamustine, fludarabin and single rituximab).

In conclusion, the OS in WM patients is affected by many other causes than disease- and treatment related factors and should guide the choice of treatment. In the oldest cohort the majority died of non-lymphoma reasons. The difference in comorbidity between males and females may influence the prognosis.

Figure 1. Cumulative probabilities of lymphoma and other cause of death stratified by sex, and age, among patients diagnosed with WM for the years 2000-2019.

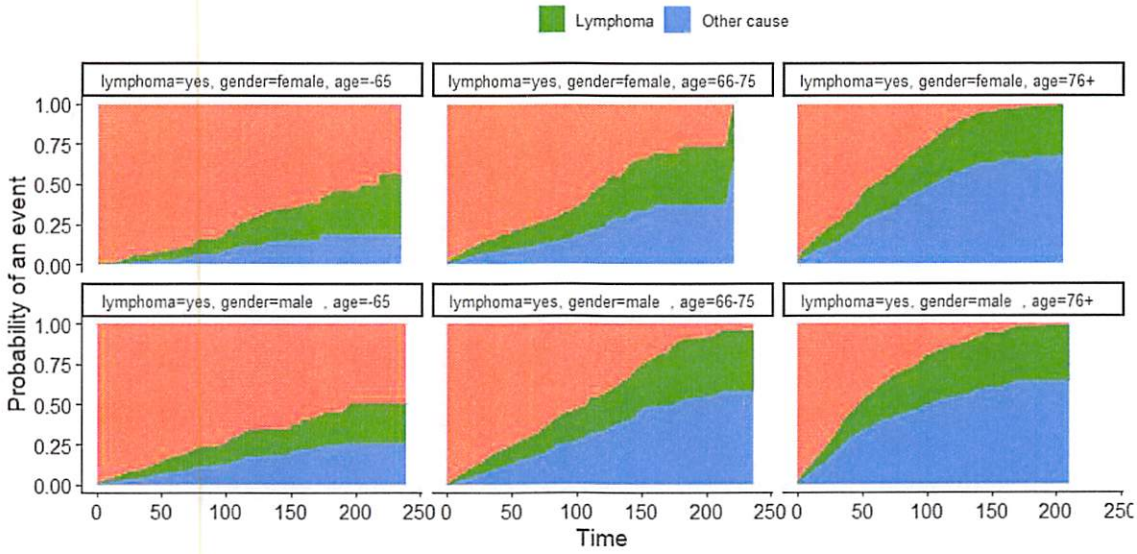
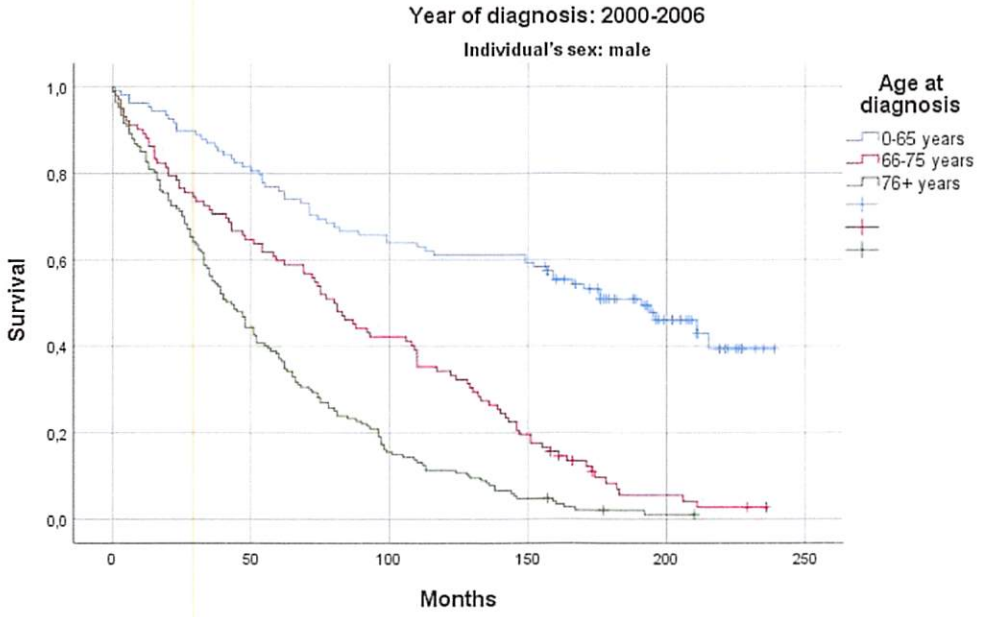
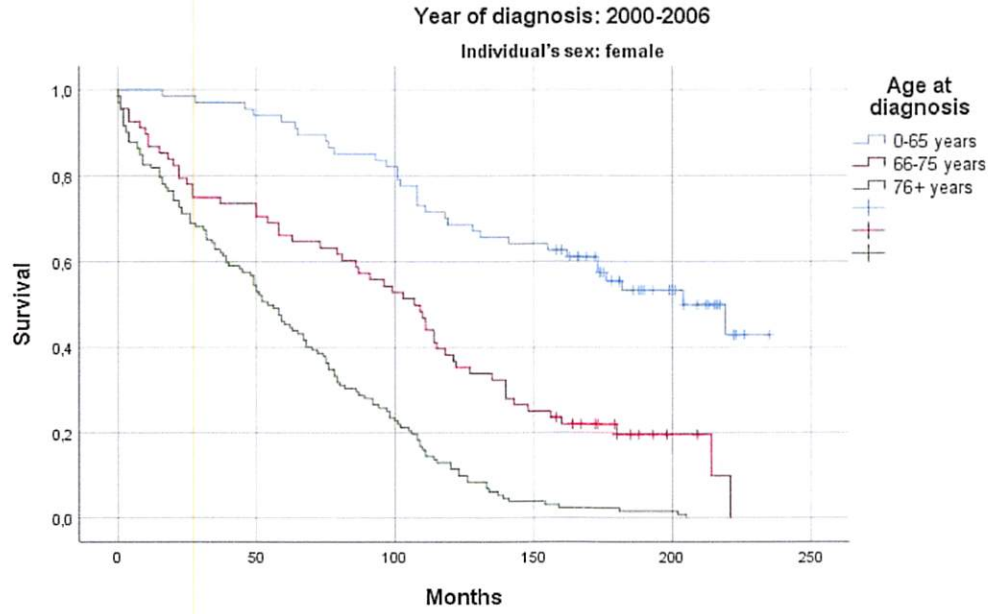
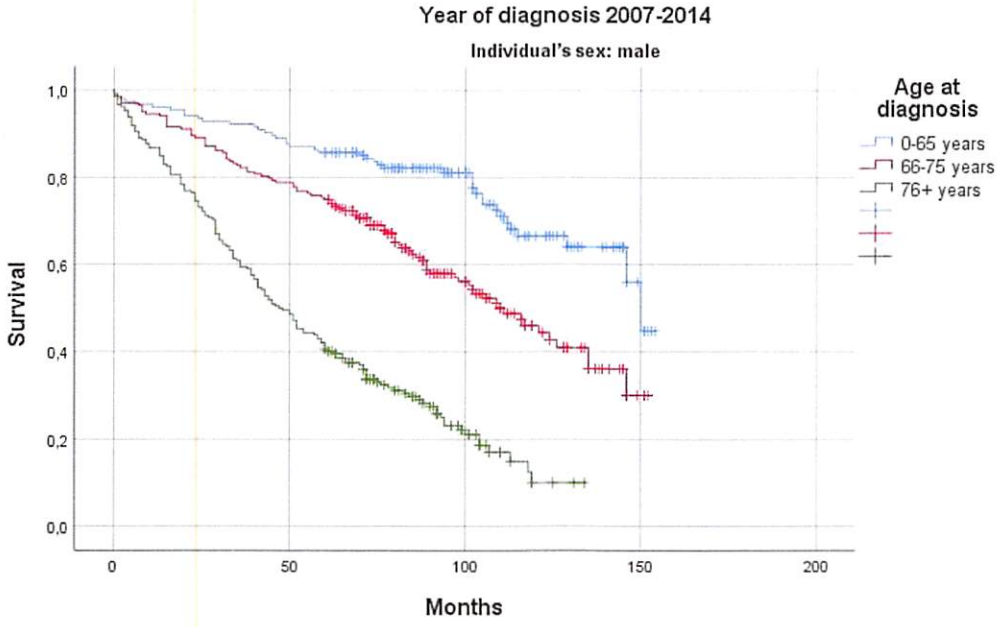
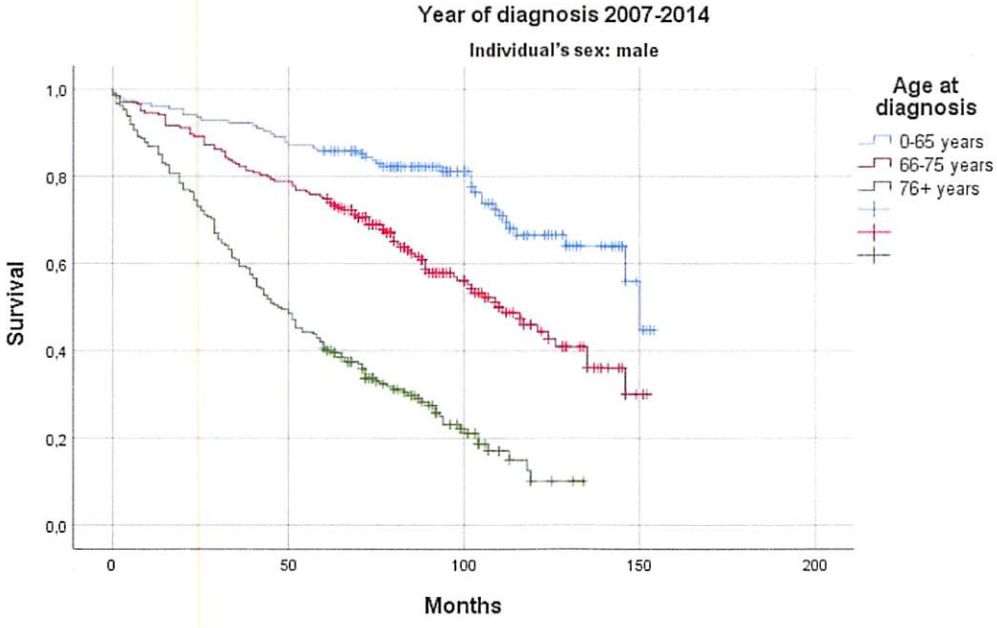


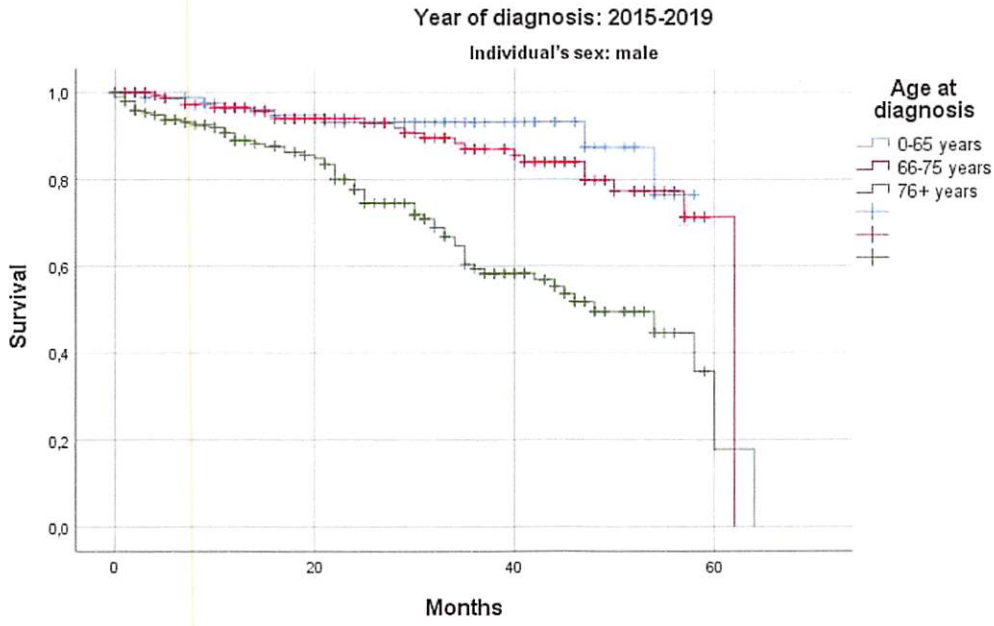
Figure 2. Kaplan-Meier curves for overall survival (OS) for males and females ≤65 years, 66-75 years, and ≥76 years and for the time periods 2000-2006, 2007-2014, and 2015-2019.






Year of diagnosis 2007-2014
Individual's sex: male
Survival
1,0
0,8
0,6
0,4
0,2
0,0
0
50
100
150
200
Months
Age at diagnosis
0-65 years
66-75 years
76+ years


Year of diagnosis 2007-2014
Individual's sex: male
Survival
1,0
0,8
0,6
0,4
0,2
0,0
0
50
100
150
200
Months
Age at diagnosis
0-65 years
66-75 years
76+ years


Year of diagnosis: 2015-2019
Individual's sex: male
Survival
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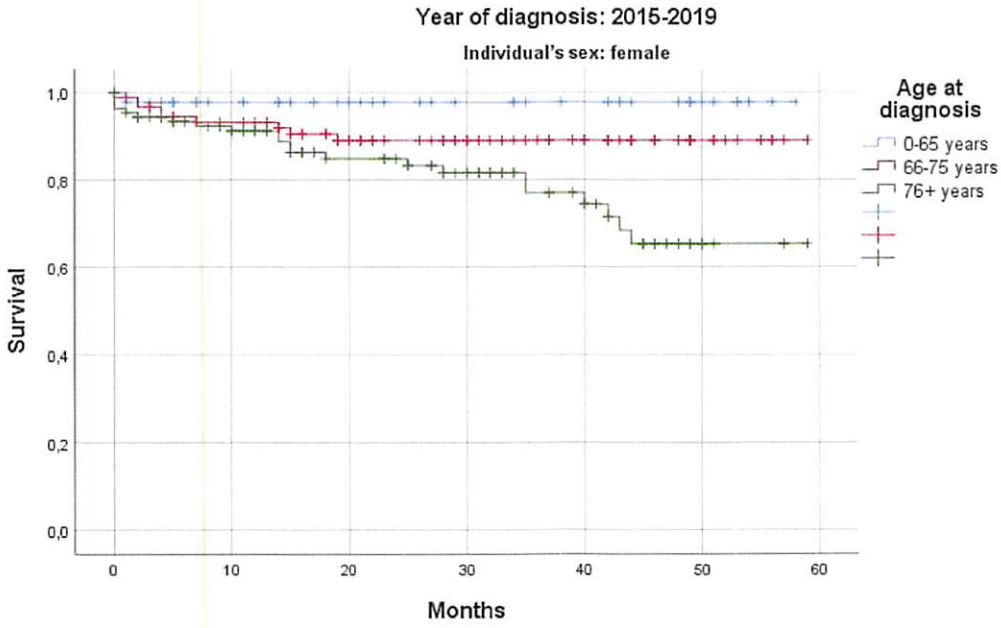
0,8
0,6
0,4
0,2
0,0
0
20
40
60
Months
Age at diagnosis
0-65 years
66-75 years
76+ years


Year of diagnosis: 2015-2019
Individual's sex: female
Survival
1,0
0,8
0,6
0,4
0,2
0,0
0
10
20
30
40
50
60
Months
Age at diagnosis
0-65 years
66-75 years
76+ years