Form record received

International Workshop on Waldenstrom's Macroglobulinemia <pattersonkent@outlook.com>
Sat 7/6/2024 4:20 AM
To:Patterson, Christopher <Christopher_Patterson@DFCI.HARVARD.EDU>

Record saved to database with ID: 90

Form ID: 1
Form title: Abstract Submission
Form name: Abstract_Submission
Submitted at: 2024-07-06 04:19:29
Submitter IP: 95.232.147.241
User-ID: 0
Username: -
User full name: -
Submitter provider: Unknown
Submitter browser: Mozilla/5.0 (Windows NT 10.0; Win64; x64) AppleWebKit/537.36 (KHTML, like Gecko) Chrome/125.0.0.0 Safari/537.36 Edg/125.0.0.0
Submitter operating system: win

First Name: Gianmarco
Last Name: Favrin
Email: gianmarco.favrin01@universitadipavia.it
Registration Type: Delegate
Abstract Title: Free Light Chain (FLC) Ratio is an Independent Risk Factor for Progression to Symptomatic Waldenstrom's Macroglobulinemia in Patients with IgM Monoclonal Gammopathy of Undetermined Significance, IgM-related disorders or Aymptomatic Waldenstrom's Macroglobulinemia
Select abstract file to attach:
/home/dkwolfpk2016/public_html/waldenstromsworkshop/media/breezingforms/uploads/abstractflciwwm2024def.docx
Please consider me for a YIA grant: YIA Grant Consideration
Conference: IWWM12

Free Light Chain (FLC) Ratio is an Independent Risk Factor for Progression to Symptomatic Waldenstrom's Macroglobulinemia in Patients with IgM Monoclonal Gammopathy of Undetermined Significance, IgM-related disorders or Aymptomatic Waldenstrom's Macroglobulinemia

Gianmarco Favrin,[1] Emilia Cappello,[1] Virginia Valeria Ferretti,[2] Sara Rattotti,[3] Claudio Cartia,[3] Giulia Vittoria Facchetti,[1] Luca Arcaini,[1,3] Marzia Varettoni[3]

[1]Department of Molecular Medicine, University of Pavia, Italy; [2]Biostatistics and Clinical Trial Center, Fondazione IRCCS Policlinico San Matteo, Pavia, Italy; [3]Division of Hematology, Fondazione IRCCS Policlinico San Matteo, Pavia, Italy

Background. Free light chains (FLC) have a well-established prognostic role in multiple myeloma, whereas their significance in patients with Waldenstrom's Macroglobulinemia (WM) or IgM monoclonal gammopathies is less clear.

Aim. We hypothesized that an abnormal monoclonal serum FLC ratio is associated with an increased risk of progression to symptomatic WM in patients with IgM-MGUS, IgM-related disorders or asymptomatic WM. Furthermore, we sought to evaluate whether in patients with symptomatic WM an abnormal FLC ratio impacts overall survival (OS).

Methods. We reviewed a prospectively maintained database including 527 consecutive patients, diagnosed and followed at the Division of Hematology of Fondazione IRCCS Policlinico San Matteo between 2000 and 2023. Serum FLC concentration was measured with a latex-enhanced immunoassay (The Binding Site, Birmingham, UK). The normal range for kappa/lambda ratio was 0.26-1.65. Patients were classified as IgM-MGUS, IgM-related disorders, asymptomatic or symptomatic WM according to the diagnostic criteria established at the second International Workshop on WM (Owen et al 2003).

Statistical analysis. OS was defined as the time between diagnosis and death for any cause or last follow-up. Progression was defined as the time between diagnosis and progression to symptomatic WM (event) or death/last follow-up. The effect of FLC on progression and OS was evaluated by multivariable proportional hazard Cox regression model and by multivariable Fine&Gray regression model for competing events, respectively. Parameters with a p-value<0.1 at univariable analysis entered multivariable models. Two sided type I error was set at 5%. All statistical analyses were performed using Stata 18 (StataCorp. 2023. Stata Statistical Software: Release 18. College Station, TX: StataCorp LLC)

Results. Baseline serum FLC were available in 316 patients, including 176 with IgM-MGUS or IgM-related disorder, 88 asymptomatic WM and 52 symptomatic WM. Their baseline characteristics are shown in Table 1. The light-chain type was kappa in 245/316 patients (77.6%). An abnormal FLC ratio (κ/λ ratio <0.26 or >1.65) was detected in 58/176 (33%) patients with IgM-MGUS/IgM-related disorder, 61/88 (69%) patients with asymptomatic WM and 40/52 (77%) patients with symptomatic WM. The median follow-up of patients was 10 years (IQR: 6-14 years). The 10-year cumulative incidence of progression was higher in patients with an abnormal versus normal FLC ratio, both in IgM-MGUS/IgM-related disorders (15.3%, 95%CI: 7.1-26.5% *vs* 4.7% 95%CI: 1.7-10%,

Pepe&Mori test p=0.023) and in asymptomatic WM (41.0%, 95%CI: 26.2-55.3% *vs* 30% 95%CI: 11.9-50.7%, Pepe&Mori test p=0.09) (Figure 1). At univariable analysis, an abnormal FLC ratio was associated with a higher risk of progression (subdistribution hazard ratio, SHR=3.9, 95%CI: 2.1-7.2, p<0.001) as well as diagnosis (asymptomatic WM vs IgM-MGUS/IgM-related disorder), reduction of polyclonal IgG (<800 vs ≥800 mg/dL), size of monoclonal component (MC) (≥1.5 vs <1.5 g/dL), hemoglobin (<12 vs ≥12 g/dL). After adjusting for diagnosis, reduction of polyclonal IgG, size of MC and hemoglobin, abnormal FLC ratio still retained its prognostic impact on progression (SHR=2.2, 95%CI: 1.1-4.5, p=0.029). FLC ratio did not impact OS (Figure 2).

Conclusions. In this study, an abnormal FLC ratio was an independent risk factor for progression to symptomatic WM in patients with IgM-MGUS, IgM-related disorders or asymptomatic WM.

Table 1. Baseline patients' characteristics

	MGUS/ IgM-RD (n=176)	Asymptomatic WM (n=88)	Symptomatic WM (n=52)	P value
Age ≥65 years, n. of patients (%)	87 (49.4%)	49 (55.7%)	31 (59.6%)	0.350
Male gender, n. of patients (%)	104 (59.1%)	54 (61.4%)	31 (59.6%)	0.950
Absolute lymphocyte count (x10^9/L)	1.95 (1.53-2.47)	2.08 (1.43-2.89)	1.90 (1.5-2.49)	0.560
Hemoglobin (g/dL), median (range)	14 (13-15)	13 (12-14)	11 (9-13)	<0.001
Platelets (x10^9/L)	240 (199-272)	257 (199-307)	249 (218-331)	0.032
Serum albumin (g/dL), median (range)	4 (4-4)	4 (4-4)	4 (3-4)	<0.001
β2-microglobulin>3000 mg/L, n. of patients (%)	18 (11.4%)	25 (32.1%)	32 (66.7%)	<0.001
Type of light chain				0.021
kappa	131 (74.4%)	76 (86.4%)	38 (73.1%)	
lambda	45 (25.6%)	11 (12.5%)	13 (25.0%)	
kappa+lambda	0 (0.0%)	1 (1.1%)	1 (1.9%)	
Serum monoclonal protein (g/dL), median (range)	1 (0-1)	1 (1-2)	2 (1-4)	<0.001
IgM level (mg/dL), median (range)	444 (286-888)	1650 (705-2573)	2210 (939-4160)	<0.001
IgG <800 mg/dL, n. of patients (%)	35 (21.5%)	31 (38.3%)	30 (66.7%)	<0.001
IgA <80 mg/dL, n. of patients (%)	15 (9.3%)	30 (37.0%)	27 (58.7%)	<0.001
Positive Bence-Jones proteinuria, n. of patients (%)	42 (25.9%)	45 (53.6%)	32 (68.1%)	<0.001
Abnormal FLC ratio, n.of patients (%)	58 (33.0%)	61 (69.3%)	40 (76.9%)	<0.001

Figure 1. Cumulative incidence of progression to active WM in patients with IgM-MGUS/IgM-related disorders (A) and in patients with asymptomatic WM (B) according to FLC ratio

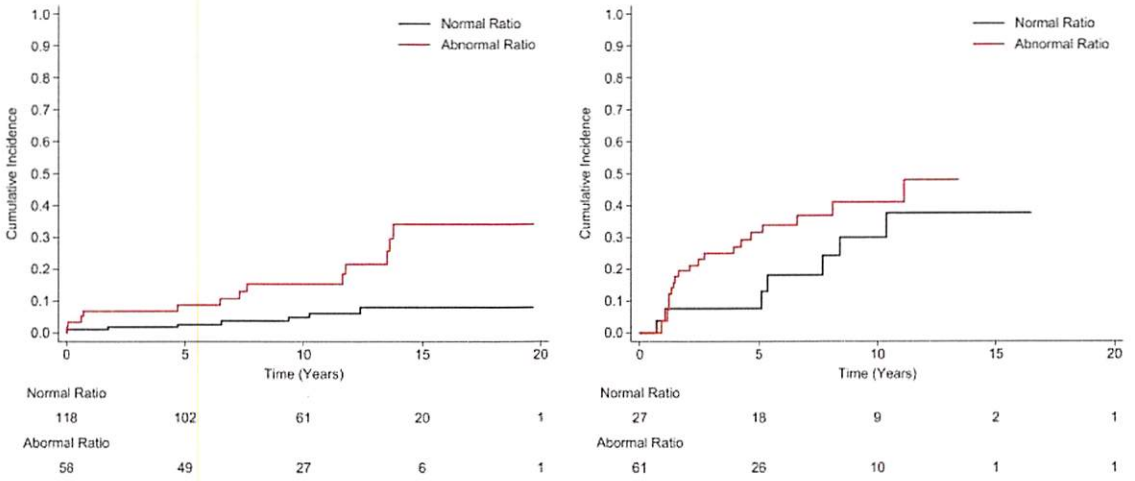

Figure 2. Overall survival in patients with IgM-MGUS/IgM-related disorders (A), asymptomatic WM (B) or symptomatic WM (C) according to FLC ratio