



Impact of Stratification of Levels of Serum Lactate Dehydrogenase (LDH) at Diagnosis on Overall Survival (OS) in Newly Diagnosed Multiple Myeloma (NDMM)

Laura A. Evans 1, 2* , Shaji K. Kumar 1 , Angela Dispenzieri 1 , Francis K. Buadi 1 , David Dingli 1 , Martha Q. Lacy 1 , Suzanne R. Hayman 1 , Prashant Kapoor 1 , Taxiarchis V. Kourelis 1 , Eli Muchtar 1 , Ronald S. Go 1 , Rahma Warsame 1 , Nelson Leung 1 , Miriam Hobbs 1 , Y. Lisa Hwa 1 , Amie Fonder 1 , Robert A. Kyle 1 , Morie Gertz 1 , S. Vincent Rajkumar 1 , Wilson I. Gonsalves 1
1 Mayo Clinic, Rochester, MN, USA, 2 Johns Hopkins University, Baltimore, MD, USA

BACKGROUND

An elevated serum LDH level is an adverse prognostic factor in NDMM. However, this category includes quantitative serum LDH levels that range from just over the upper limit of normal (ULN) to levels that may be 2 or more-fold higher than the ULN. This binary classification of serum LDH level of “normal versus elevated” fails to discriminate between the different disease biology that exists among NDMM patients with elevated serum LDH levels. Thus, we attempted to further stratify NDMM patients by the level of their serum LDH and determine its impact on OS

METHODS

The cohort included patients diagnosed with NDMM from the Mayo Clinic, Rochester from 2003 - 2017 who were treated with novel agent induction therapy and had serum LDH levels measured at the time of diagnosis. The serum LDH levels were stratified into three levels: Normal (LDH < 222 U/L), Elevated (LDH 223-444 U/L), and Very Elevated (LDH >444 U/L or >2x upper limit of normal). Survival analysis was performed using the Kaplan-Meier survival analysis and compared via the log-rank method.

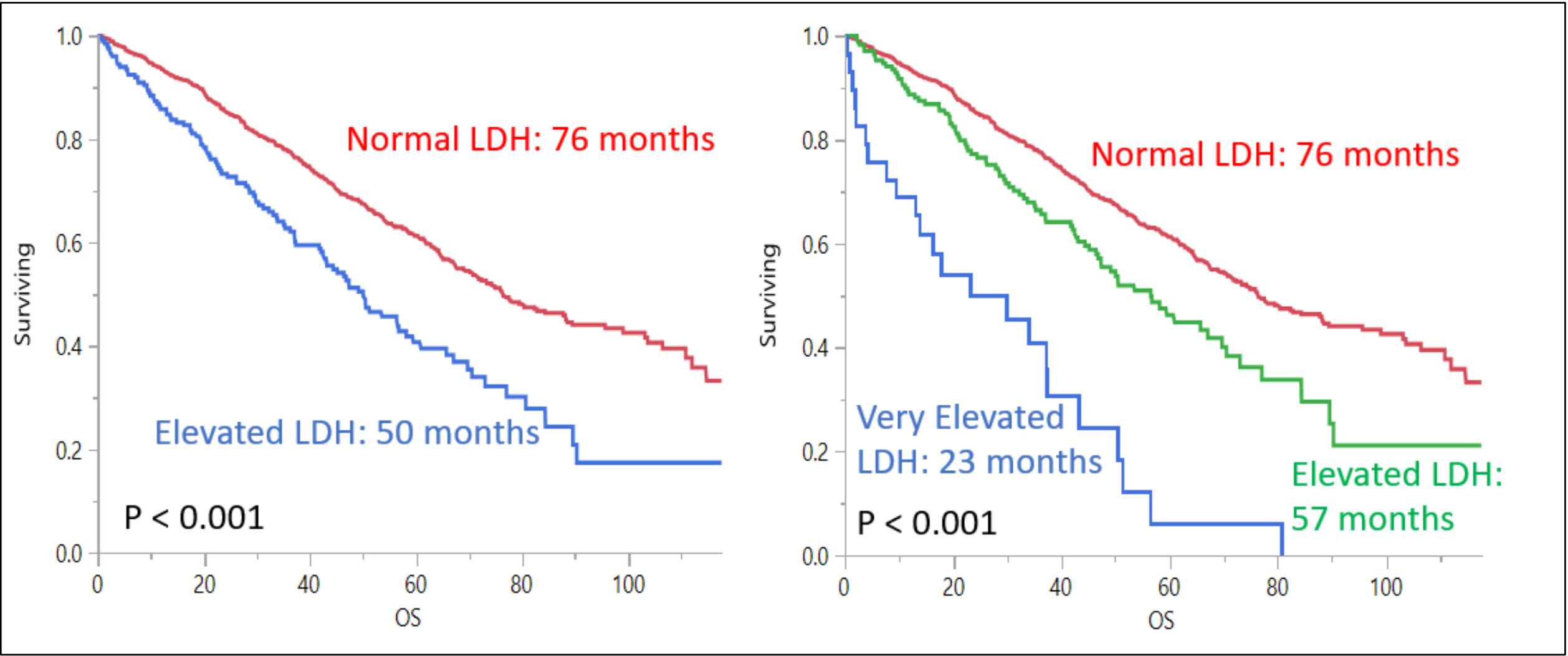
RESULTS

The cohort consists of 1,196 NDMM patients with a median age of 65 (22 – 95). R-ISS classification and cytogenetic risk were available for 968 and 970 patients respectively. The median serum LDH level was (162 U/L (3- 1260)) and an elevated LDH was present in 199 patients (17%). The median OS for patients with normal (N = 997; 83%), elevated (N = 170; 13%) and very elevated (N = 29; 3%) LDH levels were 76 months, 57 months and 23 months respectively (P < 0.001). The impact of these different levels of LDH on OS by R-ISS stage and cytogenetic risk is shown in the **Table**.

CONCLUSION

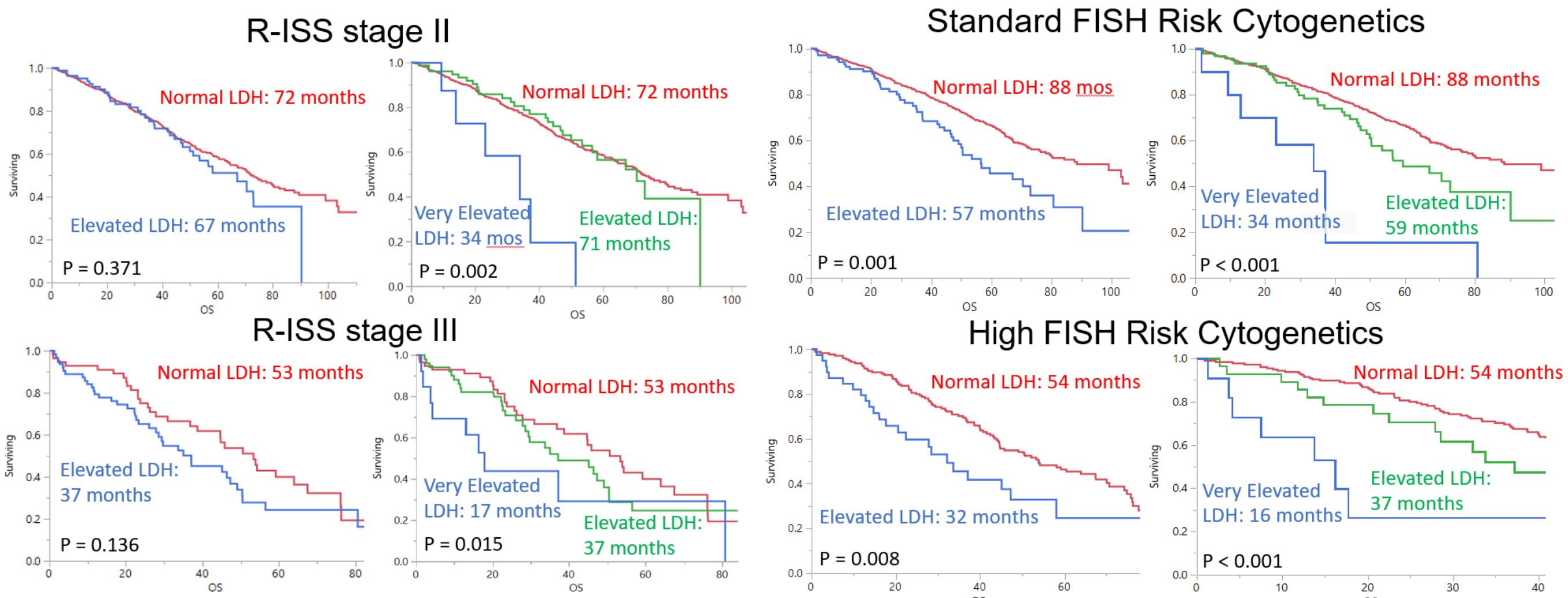
A very small subset of NDMM patients has very elevated LDH levels that confer an exceptionally poor OS irrespective of R-ISS stage and cytogenetic risk. Future studies elucidating their disease biology responsible for such poor OS outcomes are warranted.

VARIED STRATIFICATION LEVELS – BINARY SCORING AND ALTERNATIVE SCORING



The serum LDH were stratified into two and three levels for original and updated scoring, respectively.
Left: Normal (LDH < 222 U/L) (N = 997; 83%) and Elevated (LDH 223-444 U/L) (N = 199; 17%)
Right: Normal (LDH < 222 U/L) (N = 997; 83%), Elevated (LDH 223-444 U/L) (N = 170; 13%), and Very Elevated (LDH >444 U/L or >2x upper limit of normal) (N = 29; 3%).

VARIED STRATIFICATION LEVELS – EFFECT ON R-ISS AND FISH RISK SCORE



The varied stratified serum LDH levels, based on effect with R-ISS staging as well as cytogenetic risk scoring.

Level of LDH among subgroups	N	Median OS	p-value
R-ISS Stage 2			
Normal	556	72 months	P = 0.0022
Elevated	75	70 months	
Very Elevated	8	34 months	
R-ISS Stage 3			
Normal	56	53 months	P = 0.0149
Elevated	50	37 months	
Very Elevated	13	18 months	
Standard risk cytogenetics			
Normal	652	88 months	P < 0.0001
Elevated	93	59 months	
Very Elevated	10	34 months	
High risk cytogenetics			
Normal	176	54 months	P < 0.0001
Elevated	28	37 months	
Very Elevated	11	16 months	