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The Role of Gender in the Survival of Patients with Light Chain (AL) Amyloidosis with Cardiac Involvement

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A. Study Purpose and Rationale

Systemic light-chain (AL) amyloidosis is a disease that involves the deposition of light-chain immunoglobulins associated with plasma cell dyscrasia. The light-chain proteins will deposit in various tissues such as the liver, kidneys, nervous tissue, and the heart.[1] Infiltration of the heart portends a particularly poor prognosis with a median survival of 12 months at the onset of diagnosis, and 9 months when a patient presents with signs of congestive heart failure.[2]

Several studies have been performed to determine the possible risk factors and predictors of survival for patients with cardiac amyloidosis. Specifically troponin I and septal thickness have been shown to be predictive of survival.[3] Interestingly, gender has also been suggested as a possible predictor of survival in light chain amyloidosis. In one such study the researchers looked at patients with light-chain amyloid with cardiac involvement that were not candidates for stem cell transplant.[4] Patients were divided up based on gender, troponin levels, interventricular septal thickness, age, and response to treatment. Survival curves showed superior survival for lower troponin, smaller septal thickness and partial or complete remission status. Additionally, this study found that woman survived significantly longer when compared to men. In an effort to determine what might cause a gender discrepancy, another study was done that directly compared several physiological heart parameters between men and woman with AL amyloid. The results from this paper found no significant difference between the two genders.[5] However, this study did not address any differences in mortality between the two groups.

To date there does not appear to be a study that specifically determines if gender is an independent variable for survival. The purpose of this study is to see if gender is an independent predictor for survival in relation to previously determined risk factors.

B. Study Design and Statistical Analysis

A retrospective chart review will be done to identify and collect patient data for analysis. The initial objective will be to try and create survival curves similar to those seen in D. Lebovic et al, 2008. The charts will be reviewed to find all patients in the records of

Columbia University Medical Center that have light-chain amyloidosis with cardiac involvement. From the patient's that have light chain amyloidosis with cardiac involvement, the data points that will be gathered include: gender, troponin levels, interventricular septal thickness, and age. The response to treatment will also be collected in a way that has been previously described.[6] Men and Woman will be divided into separate groups, troponin I levels separated between levels of >0.12 and <0.12, Interventricular septal thickness will be separated between > 0.14 cm and < 0.14 cm, age >70 and <70 years old, and response to treatment will be divided as no response, partial, or complete response. These cut-offs will be taken from the D. Lebovic 2008 study. Kaplan Meier curves will be created in relation to the variables mentioned and a logrank test will be used for comparison. These Kaplan Meier curves will be compared to the D. Lebovic et al, 2008 study. Patient that were included in the initial D. Lebovic study will be excluded from this portion of the study as well as any patients that had a stem cell transplant or heart transplant.

The second part of the study will combine all of the patients with light chain amyloid with cardiac involvement that have not undergone stem cell transplant or heart transplant. The variables from the first half of the study will be added to the extra variables of brain-natriuretic peptide and left ventricular ejection fraction. Then Multivariate analysis will be performed on these variables using Cox proportional Hazards Model with the goal of determining if gender is independent of any of these given variables.

C. **Study Procedure**
This is a retrospective chart review the will require going through patient's electronic medical records to extract the data points. Patient's date of death will be confirmed using the Social Security Death Index. The review will also require confirming which patients were included in the previous D. Lebovic study in order to not include them in the initial analysis. No new procedures need to be performed on the patient's studied.

D. Study Drugs
None

E. Medical Devices
None

F. Study Questionnaires
None

G. Study Subjects

Inclusion criteria:
1) All patients that have confirmed light chain (AL) amyloidosis with cardiac involvement.

Exclusion criteria:

1) The first part of the study will exclude patients that participated in the previous study mentioned, but will be included in the second half of the study.
2) Patient's that were given a stem cell or heart transplant.

H. Recruitment of Subjects
Patients will be recruited in the retrospective analysis by the criteria stated above. The collection of the data is very unlikely to affect the patients and it is unlikely that patient consent would be needed.

I. Confidentiality of Study Data
All data will be collected and stored on a password secured computer with a password secured file that is accessible only to the researchers involved. Patient will be given a unique five digit number to replace their name as an identifier.

J. Potential Conflict of Interest
None

K. Location of the Study
New York Presbyterian - Columbia University Medical Center

L. Potential Risks
None

M. Potential Benefits
The study subjects will not directly benefit from the study. However, the data gathered from these subjects may help us better predict prognosis for patients and tailor therapy appropriately

N. Alternative Therapies
Not Applicable

O. **Compensation to Subjects**
None

P. Costs to Subjects
None

Q. Minors as Research Subjects
None

R. Radiation or Radioactive Substances
None

References
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112 (13): 2047-60.
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4) Lebovic D, et al. Predictors of survival in patients with systemic light-chain amyloidosis and cardiac involvement initially ineligible for stem cell transplantation and treated with oral melphalan and dexamethasone. British Journal of Hematology. 2008; 143(3): 369-73.
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