

INPLASY PROTOCOL

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The clinical characteristics of immunoglobulin light chain amyloidosis in Chinese population: A systematic scoping review

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Review question / Objective: To understand the clinical characteristics of Immunoglobulin light chain (AL) amyloidosis in Chinese population and identify future research gaps.

Information sources: We will conduct a systematic search in the databases of PubMed, EMBASE and CNKI. The following items will be used to develop our search strategy: "amyloidosis", "amyloidosis*" "amyloido*", "AL amyloidosis", "China".

Main outcome(s): 1. Overview of the publication landscape and patient volume at different time periods and regions of those included literatures; 2. Characteristics of Chinese patients with AL Amyloidosis, including: (1) Demographic characteristics: Age, gender, time to diagnosis/treatment, isotype, organ involvement, etc. (2) Physicochemical indexes: dFLC, eGFR, NT-proBNP, TnT, serum creatinine and 24 hours urinary protein.

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 24 September 2021 and was last updated on 24 September 2021 (registration number INPLASY202190086).

INTRODUCTION

Review question / Objective: To understand the clinical characteristics of Immunoglobulin light chain (AL) amyloidosis in Chinese population and identify future research gaps.

Rationale: To describe the clinical characteristics of AL Amyloidosis in China, we will conduct a systematic search in the databases of PubMed, EMBASE and CNKI using search terms "amyloidosis", "amyloidosis*" "amyloido*", "AL amyloidosis" and "China". and limit the search results to only literatures published in the past 10 years. Case reports, re-

views, consensus, thesis and questionnaires will be excluded in this study and we will separately analyze the non-interventional studies and interventional studies to ensure the homogeneity of analysis. We will describe the clinical characteristics of AL amyloidosis in China. The scoping review will be performed according to the preferred reporting items for scoping review (PRISMA) extension statement. We will include literatures that reported Chinese patients with AL amyloidosis and extract the baseline characteristics of patients from each included article.

1. Describe the publishing landscape, research hotspot, patient volume and patient distribution of AL Amyloidosis in China.
 - (1) Sample distribution: Number of patients in different regions of China.
 - (2) Number of literatures/sample size across years.
2. Describe the characteristics of enrolled patients as followings:
 - (1) Demographic characteristics, e.g., age, gender, isotype (κ or λ), newly diagnosed or relapsed/refractory (proportion), primary or secondary disease, time from signs to diagnosis, time from diagnosis to treatment, etc.
 - (2) Clinical characteristics, e.g., organ involvement (type and number), stages of heart failure (NYHA), percentage of bone marrow plasma cells, etc.
 - (3) Clinical parameters at baseline, e.g., dFLC (50mg/L and 180mg/L as threshold), eGFR (50 mL/min/1.73 m² as threshold), NT-proBNP, TNT, 24-hour proteinuria, etc.

Condition being studied: AL amyloidosis is the most common type of systemic amyloidosis which is characterized by a clonal population of bone marrow plasma cells that produces a mono-clonal light chain of κ or λ type as either an intact molecule or a fragment. This insoluble protein deposits in tissues and interferes with organ function. The incidence of amyloidosis is not well documented, but probably falls between 5 and 13 per million per year. One literature conducted in France reported that the yearly incidence of AL amyloidosis is 12.5 (95%CI, 5.6 – 19.4) cases per million inhabitants. The nationwide epidemiological data for AL amyloidosis in China is lacking. Moreover,

the specific situation of Chinese patients with AL amyloidosis is still unclear. The relevant guidelines and consensus are mainly based on European and American research, and there is a lack of data on clinical epidemiology, diagnosis and treatment of domestic patients. This situation brings great difficulties to doctors in clinical practice. First of all, there is a serious lack of understanding of the incidence and prevalence of the disease. Many doctors do not have a clear cognition of the disease, which can easily lead to missed diagnosis. Secondly, doctors are unaware of the organs that may be affected by AL amyloidosis and the impact of this disease on organ functions, so they sometimes even cannot prescribe appropriate examinations and tests for potential patients, not to mention the proper assessment of the patient's condition. Thirdly, there is insufficient understanding of the prognosis of Chinese patients with AL amyloidosis, and it is impossible to predict the outcome of the patients based on clinical presentation. Due to the absence of epidemiological and clinical characteristics and outcomes of AL Amyloidosis in China based on either national-wise or multi-center study. This scoping review aims to systematically search and analyze published data to understand the current situation of AL amyloidosis in China that having been assessed by evidence and identify future research gaps.

METHODS

Search strategy: 1. embase #1. 'AL amyloidosis'/exp OR ("light-chain" NEAR/3 amyloidos* OR AL NEAR/3 amyloidos*):ab,ti,kw | #2. 'China'/exp OR China OR (Chinese OR Taiwan OR Hongkong OR Hongkong OR Macau OR Macao OR Beijing OR Shanghai OR Tianjin OR Chongqing OR Inner Mongolia OR Tibet OR Guangxi OR Sinkiang OR Ningxia OR Xinjiang OR Hebei OR Shanxi OR Liao-ning OR Jilin OR Heilongjiang OR Jiangsu OR Zhejiang OR Anhui OR Fujian OR Jiangxi OR Shandong OR Henan OR Hubei OR Hunan OR Guangdong OR Hainan OR Sichuan OR Guizhou OR Yunnan OR

Shaanxi OR Gansu OR Qinghai):ab,ti,ff | #3. #1 AND #2 | 2. Pub Med #1. "Immunoglobulin Light-chain Amyloidosis"[Mesh] OR ("Light chain"[tiab] AND Amyloidos*[tiab]) OR "AL amyloidos*"[tiab] OR "Amyloidosis AL"[tiab] | #2. "China"[Mesh] OR China OR Chinese OR Taiwan OR Hong kong OR Hongkong OR Macau OR Macao OR Beijing OR Shanghai OR Tianjin OR Chongqing OR Inner Mongolia OR Tibet OR Guangxi OR Sinkiang OR Ningxia OR Xinjiang OR Hebei OR Shanxi OR Liaoning OR Jilin OR Heilongjiang OR Jiangsu OR Zhejiang OR Anhui OR Fujian OR Jiangxi OR Shan-dong OR Henan OR Hubei OR Hunan OR Guangdong OR Hainan OR Sichuan OR Guizhou OR Yunnan OR Shaanxi OR Gansu OR Qinghai | #3. #1 AND #2 | 3. CNKI (期刊、学位、会议, 中英文扩展: 否) | #1. SU%=轻链淀粉样变性+轻链淀粉样变性病+轻链淀粉样变+轻链型淀粉样变性+轻链型淀粉样变性病+轻链型淀粉样变 OR TKA=轻链型 /NEAR 3 淀粉样变 OR 轻链型 / NEAR 3 淀粉样变性 OR 轻链型 /NEAR 3 淀粉样变性病 OR 轻链 /NEAR 3 淀粉样变 OR 轻链 /NEAR 3 淀粉样变性 OR 轻链 /NEAR 3 淀粉样变性病.

Participant or population: AL Amyloidosis in Chinese population. Chinese population is defined as literature participants enrolled from healthcare institutions in mainland China.

Intervention: There will be no limitation.

Comparator: There will be no limitation.

Study designs to be included: Non-interventional studies and interventional studies.

Eligibility criteria: Studies enrolling patients with AL Amyloidosis in Chinese population. But we will excluded case reports, reviews, consensus, thesis and questionnaires.

Information sources: We will conduct a systematic search in the databases of PubMed, EMBASE and CNKI. The following

items will be used to develop our search strategy: "amyloidosis", "amyloidos*" "amyloido*", "AL amyloidosis", "China".

Main outcome(s): 1. Overview of the publication landscape and patient volume at different time periods and regions of those included literatures; 2. Characteristics of Chinese patients with AL Amyloidosis, including: (1) Demographic characteristics: Age, gender, time to diagnosis/treatment, isotype, organ involvement, etc. (2) Physicochemical indexes: dFLC, eGFR, NT-proBNP, TnT, serum creatinine and 24 hours urinary protein.

Quality assessment / Risk of bias analysis: We will not asses the formal quality of studies.

Strategy of data synthesis: For publishing landscape: 1. We plan to draw a literature published map to describe patient distribution in China and number of patients being diagnosed in different cities of China. For multi-center studies, we assume equal proportions of samples enrolled in each study site. 2. We also plan to draw a trajectory of number of patients being diagnosed in each year. For long enrollment period (e.g., patients were enrolled from 2002 to 2009), we assume an equal monthly enrollment number to attribute the samples into each year. Trajectory of sample size were smoothed using the LOESS (Locally Weighted Scatterplot Smooth-ing) method with the span set to 0.2. For patient characteristics 1. To analyze the clinical characteristics of AL Amyloidosis, literatures that recruited duplicate populations will be excluded. The duplicated populations were defined as study paticipants with same diagnosed disease enrolled from the same institute within same time period. For literatures analyzing data from duplicated population, we will keep the study with larger sample size. Literatures recruiting participants from the same institute but with a different study period, however, the study period is overlapped >6months will be considered as partially-duplicated population literatures. Literatures recruiting participants from the

same institute but the study period overlapped ≤ 6 months with each other will be considered as non-duplicated population literatures. The partially-duplicated and non-duplicated population literatures will be included in the data analysis. 2. When we describe the clinical characteristics of patients, we may pool the mean value of patients' characteristic (such as age) reported in each study. Data will be pooled using a fixed-effect model. Where mean values were not reported, median was used as a surrogate. 3. We will consider the representative of included samples when analysis. 4. We will analysis the biomarkers with thresholds of clinical significance (e.g., eGFR <50 ml/min/1.73m²). For study that only reported mean and standard deviation values of biomarker, we will assume its normal distribution and calculate the proportion of patients having a biomarker value less than a threshold (e.g., eGFR <50 ml/min/1.73m²) using the cumulative distribution function. All statistical analysis was performed with R.

Author 4 - Lingjie Xu collected the data, then will perform analyses.

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Subgroup analysis: No subgroup analysis.

Sensitivity analysis: No sensitivity analysis.

Country(ies) involved: China.

Keywords: AL amyloidosis; clinical characteristics; meta analysis.

Contributions of each author:

Author 1 - Chengcheng Fu drafted and revised the protocol, collected the data, then will perform or supervise analyses, provide substantive suggestions for revision or critically reviewed subsequent iterations of the manuscript.

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