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ORIGINAL ARTICLE

Exploratory bibliometric analysis and text mining to reveal research trends in cardiac aging

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Abstract

Objectives: We conducted a text mining analysis of 40 years of literature on cardiac aging from PubMed to investigate the current understanding on cardiac aging and its mechanisms. This study aimed to embody what most researchers consider cardiac aging to be.

Methods: We used multiple text mining and machine learning tools to extract important information from a large amount of text.

Results: Analysis revealed that the terms most frequently associated with cardiac aging include "diastolic," "hypertrophy," "fibrosis," "apoptosis," "mitochondrial," "oxidative," and "autophagy." These terms suggest that cardiac aging is characterized by mitochondrial dysfunction, oxidative stress, and impairment of autophagy, especially mitophagy. We also revealed an increase in the frequency of occurrence of "autophagy" in recent years, suggesting that research on autophagy has made a breakthrough in the field of cardiac aging. Additionally, the frequency of occurrence of "mitophagy" has increased significantly since 2019, suggesting that mitophagy is an important factor in cardiac aging.

Conclusions: Cardiac aging is a complex process that involves mitochondrial dysfunction, oxidative stress, and impairment of autophagy, especially mitophagy. Further research is warranted to elucidate the mechanisms of cardiac aging and develop strategies to mitigate its detrimental effects.

KEYWORDS
autophagy, cardiac aging, mitophagy

1 | INTRODUCTION

The emergence of an aging society is leading to advancements in aging research. An aging heart exhibits several physiological alterations. Unlike physical aging such as gray hair, wrinkled skin, and decreased mobility, there is no concise definition of cardiac aging, and the mechanisms underlying its complexities remain largely unknown. Several studies have characterized diastolic dysfunction as a consequence of cardiac aging, whereas fibrosis, cardiac hypertrophy, and oxidative stress have been proposed as contributing factors.[1–5] However, the heterogeneity of cardiac aging assessment perspectives has complicated the understanding of its essence (Figure S1A).

Recently, extensive research has clarified the intricacies of cardiac aging (Figure S1B), providing a pathway for elucidating its molecular underpinnings and developing strategies to mitigate its detrimental effects.

Text mining has become increasingly popular in recent years, with over 40,000 studies using text mining being available on PubMed. Text mining was originally used for commercial purposes, but it has recently been used in social medicine and in several medical researches.[6–8] Kazawa et al.[9] published a study that used text mining to summarize the consensus of experts. Other impactful original research articles that utilized text mining to analyze the PubMed database for an overview of autophagy have also been published.[10]

In this study, we used text mining to analyze 40 years of literature on cardiac aging from PubMed. We aimed to determine how cardiac aging is defined and what is considered as cardiac aging. As one software may miss some applications of text mining, we used several text mining tools in this study (Figure S1C). This study aimed to clarify the understanding of cardiac aging among researchers and assess the underlying mechanisms published in the literature.

2 | METHODS

The detailed methods are listed in the Supplemental Methods.

2.1 | Sample collection

A PubMed search was conducted using the terms "cardiac aging" OR "cardiac senescence" OR "heart aging" OR "heart senescence."

2.2 | KH coder and VOS viewer

We used KH Coder 3.Beta.07f, which has previously been used for medical research,[9,11–13] and VOS viewer 1.6.20, which can visualize networks formed by the relationships between academic studies and authors.[14,15] The list of terms excluded as nonspecific terms is presented in Table S1.

2.3 | Word cloud generator

Free Word Cloud Generator is a web-based software that facilitates word cloud visualizations of web pages, text files, or any other arbitrary text input (FreeWordCloudGenerator.com). The analysis method "Word Cloud" has been frequently used in research.[10]

2.4 | National Center for Biotechnology Information (NCBI) LitSuggest

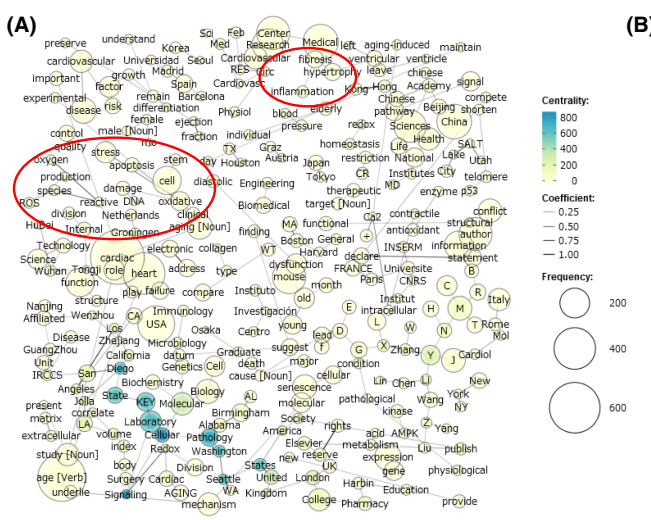
LitSuggest is a software that uses advanced machine learning techniques to recommend relevant PubMed articles with high accuracy.[16]

3 | RESULTS

3.1 | Text mining analysis of studies conducted from 1984 to 2023 using multiple tools

Before analysis, we loaded all studies conducted from 1984 to 2023 obtained via PubMed into KH Coder and performed preprocessing. First, we performed word frequency analysis and confirmed the results (Figure S2). Next, we created a co-occurrence network of terms. We revealed that the terms "ROS," "oxygen," "oxidative," "damage," and "apoptosis" were co-occurring; additionally, the terms "fibrosis," "hypertrophy," and "inflammation" were co-occurring (Figure 1A). We then constructed a self-organizing map to visualize the overall research landscape of cardiac aging. Clusters were automatically created and colored via KH Coder (Figure 1B). For multifaceted evaluation, we created a word cloud using all studies via Word Cloud Generator (Figure 1C). Additionally, using VOS viewer, all studies that matched the search criteria for cardiac aging were used to construct a bibliometric network (Figure 1D).

FIGURE 1 (A) We used KH Coder 3.Beta.07f to analyze all PubMed articles on cardiac aging from 1984 to 2023. We first constructed a co-occurrence network of terms. We found that the terms "ROS", "oxygen", "oxidative", "damage", and "apoptosis" were co-occurring; moreover, the terms "fibrosis", "hypertrophy" and "inflammation" were co-occurring in the same cluster. These terms were placed in red circles. (B) Using the same data, we constructed a self-organizing map to visualize the overall research landscape of cardiac aging. Clusters were automatically generated via KH Coder and colored accordingly. The terms indicated in red circles are characteristic terms found in studies on cardiac aging. (C) To conduct a comprehensive assessment, we used Free Word Cloud Generator (FreeWordCloudGenerator.com) to create a word cloud of all PubMed articles from 1984 to 2023. The terms "cardiac" and "aging," which were used in the PubMed search, appeared in large letters, but other terms were relatively common in studies on cardiac aging. The analysis also includes the names and institutions of the authors; hence, the terms "USA," "China," "Italy," "France," and "Japan" were also extracted. Furthermore, the term "mitochondrial" was extracted, indicating that this term appears frequently in studies on cardiac aging. (D) We also constructed a bibliometric network using VOS viewer 1.6.20 to analyze all studies that matched the search criteria for cardiac aging. Using VOS viewer, we could extract characteristic genes such as "p53" and "p16" in the yellow-colored group, which was centered on the term "senescence." In the blue-colored area, the terms "diastolic dysfunction" and "ejection fraction" were extracted, indicating that cardiac function is also being discussed in research on cardiac aging. In the green-colored area, the terms "mitochondria," "reactive oxygen species," and "ROS" are shown, which are related to the mechanisms of cardiac aging; these terms are indicated in red circles. ROS, reactive oxygen species.


(A)
Centrality:
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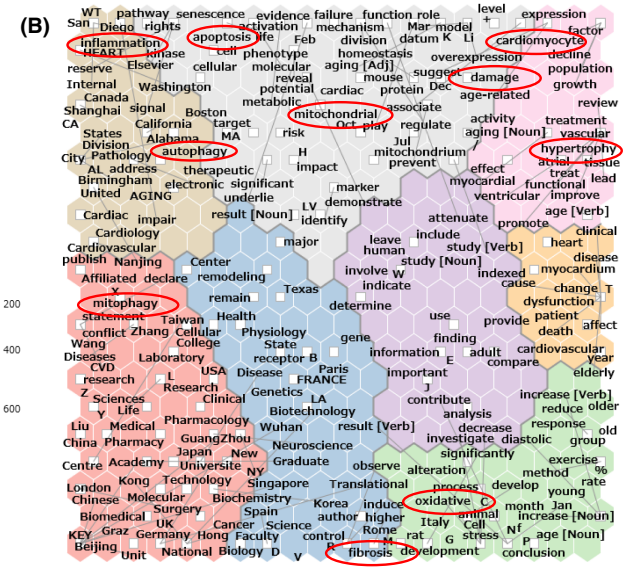
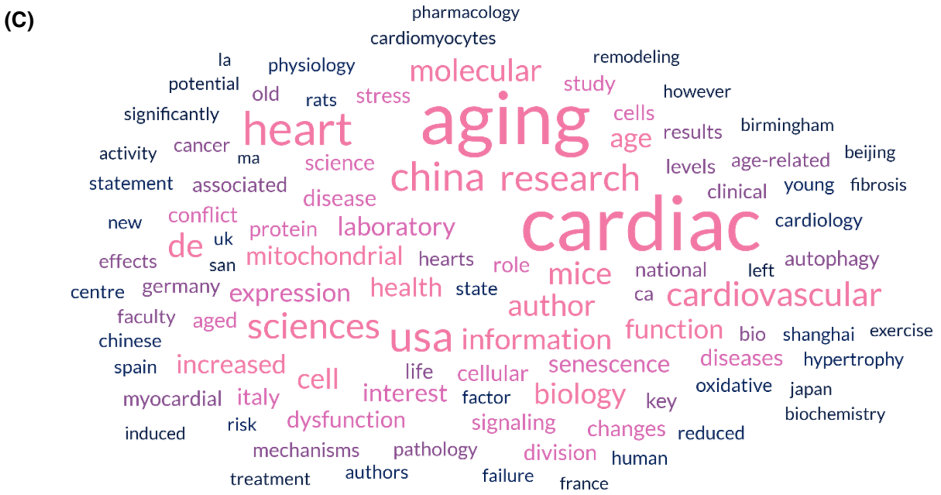
600
400
200
0
Coefficient:
0.25
0.50
0.75
1.00
Frequency:
200
400
600


(B)
inflammation
apoptosis
cardiomyocyte
damage
mitochondrial
autophagy
hypertrophy
mitophagy
fibrosis


(C)
pharmacology
cardiomyocytes
physiology
molecular
remodeling
potential
old
rats
stress
study
however
significantly
heart
aging
cells
age
results
birmingham
activity
cancer
ma
science
china research
levels
age-related
beijing
statement
associated
disease
clinical
young
fibrosis
new
conflict
protein
laboratory
cardiac
cardiology
effects
de
uk
mitochondrial
hearts
role
mice
national
autophagy
san
left
centre
germany
expression
health
state
author
ca
cardiovascular
faculty
aged
sciences
usa
information
function
bio
shanghai
exercise
chinese
spain
increased
cell
life
cellular
senescence
diseases
hypertrophy
myocardial
italy
interest
factor
biology
key
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authors
failure
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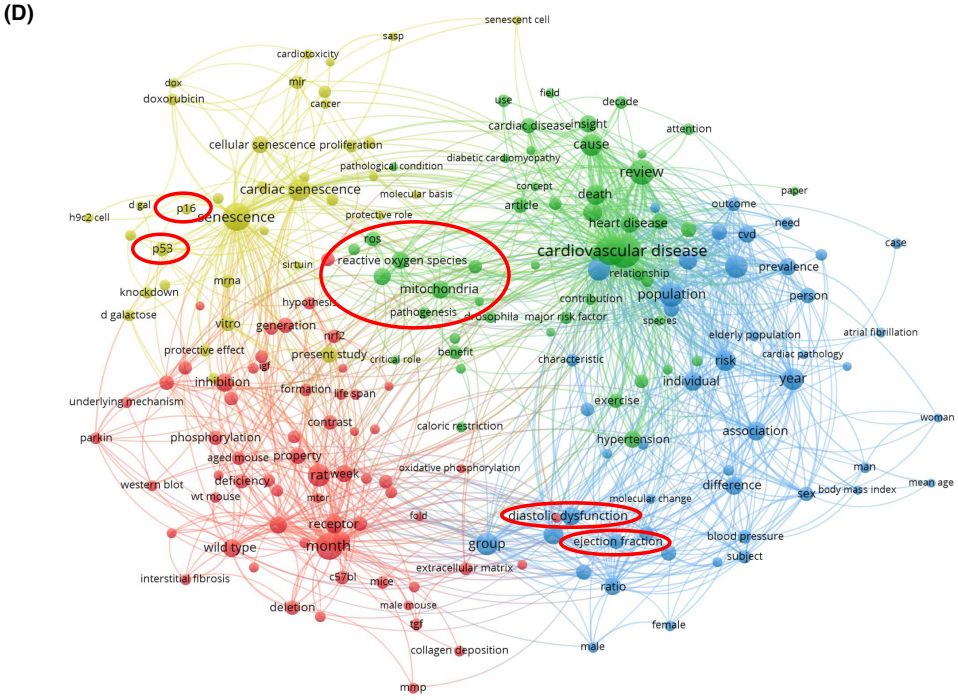
(D)
senescent cell
sasp
cardiotoxicity
dox
doxorubicin
mir
cancer
use
field
decade
cardiac disease
insight
attention
cellular senescence proliferation
cause
pathological condition
diabetic cardiomyopathy
review
cardiac senescence
concept
death
paper
molecular basis
d gal
p16
article
outcome
h9c2 cell
senescence
protective role
heart disease
need
p53
ros
cvd
case
reactive oxygen species
cardiovascular disease
sirtuin
relationship
prevalence
mrna
knockdown
mitochondria
contribution
population
person
hypothesis
d galactose
pathogenesis
drosophila
major risk factor
species
vitro
generation
elderly population
atrial fibrillation
nrf2
protective effect
present study
critical role
benefit
characteristic
risk
cardiac pathology
igf
inhibition
individual
year
formation
life span
underlying mechanism
exercise
contrast
caloric restriction
woman
association
parkin
phosphorylation
hypertension
aged mouse
property
man
oxidative phosphorylation
rat
week
difference
mean age
western blot
deficiency
sex
body mass index
wt mouse
mtor
molecular change
diastolic dysfunction
fold
receptor
blood pressure
ejection fraction
wild type
month
group
subject
extracellular matrix
interstitial fibrosis
c57bl
mice
ratio
male mouse
deletion
tgf
female
collagen deposition
male
mmp

3.2 | Evolution of research over time

A self-organizing map was constructed using the characteristic terms identified in the abovementioned analysis, their counterparts (e.g., "diastolic" and "systolic"), and terms considered important for cardiac aging (e.g., ventricular and atrial) (Figure 2A). Terms located separately indicated that they were not frequently used in the same context.

Furthermore, we used KH Coder to perform coding analysis to determine the frequency of occurrence of each term in all studies on cardiac aging, which were divided into 5-year intervals using a bubble plot (Figure 2B). As the bubble plots differed between 1984–2018 and 2019–2023, with a particular significant increase in the frequency of occurrence of mitophagy, we created word clouds for each period by dividing them into "1984–2018" and "2019–2023" (Figure 3A,B). Additionally, we constructed bibliometric networks for each period using VOS viewer (Figure 4A,B).

3.3 | Word clouds for the past 5 years using machine learning

We trained NCBI's LitSuggest on studies from "1984 to 2018." Overall, 271 studies published in the past 5 years ("2019–2023") were extracted. Of the 271 references, 261 were identified by machine learning as relevant to 1984–2018 studies on cardiac aging; a word cloud using these 261 studies was then created (Figure 5A). We also created a word cloud from the 10 studies that were excluded by artificial intelligence (AI); however, nonspecific terms appeared in the word cloud (Figure S3).

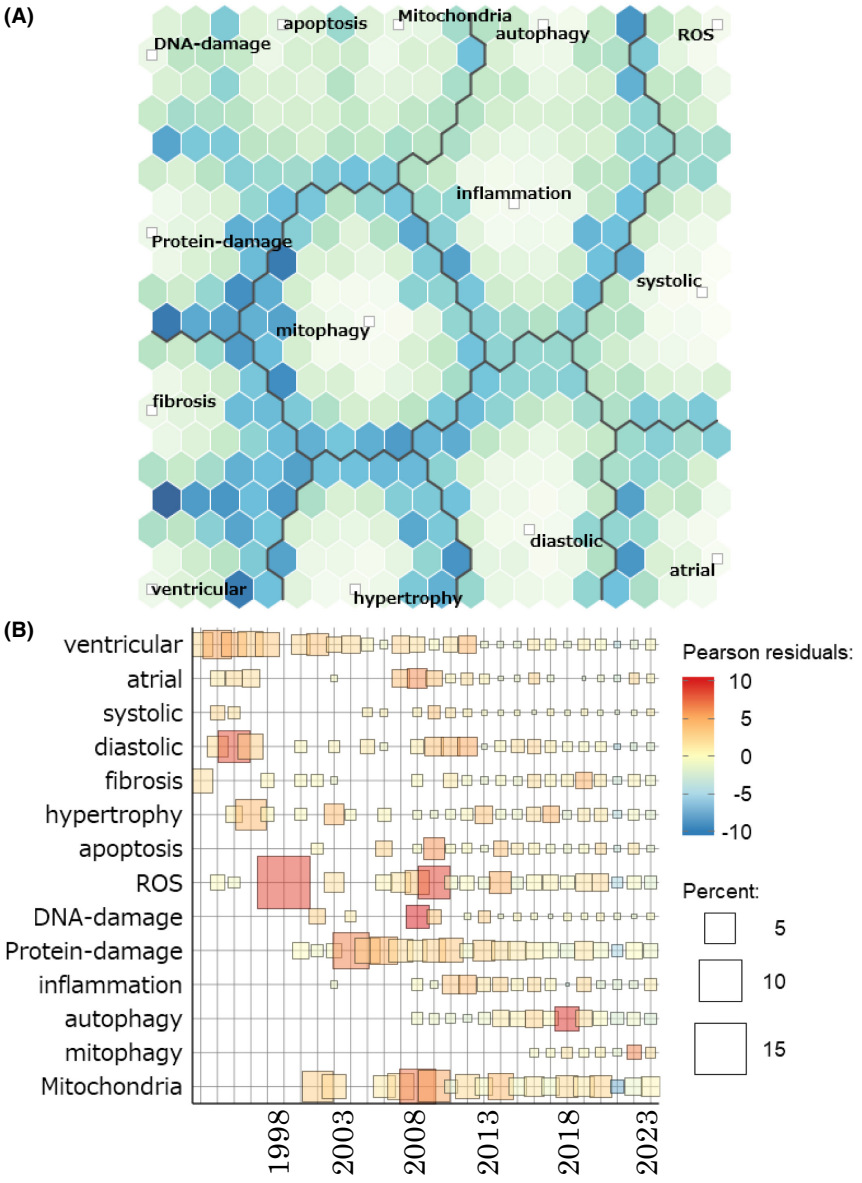

FIGURE 2 (A) We constructed a self-organizing map using the characteristic terms identified in the previous analysis (Figure 1), their counterparts (e.g., "diastolic" and "systolic"), and terms considered important for cardiac aging (e.g., ventricular and atrial). In this figure, the distance between adjacent nodes was calculated using the Euclidean distance, and the nodes were colored blue when they were far apart. The formation of a dark-blue indicated that the occurrence patterns of the term were different across that line. (B) We used KH Coder 3.Beta.07f to analyze the frequency of occurrence of each term in the entire set of studies on cardiac aging, which were divided into 5-year intervals. In this figure, the color coding was based on the Pearson residual. The darker the color of a term, the greater the frequency of the term. For example, "mitophagy" appeared more frequently than other terms in studies conducted from 2019 to 2023. ROS, reactive oxygen species.

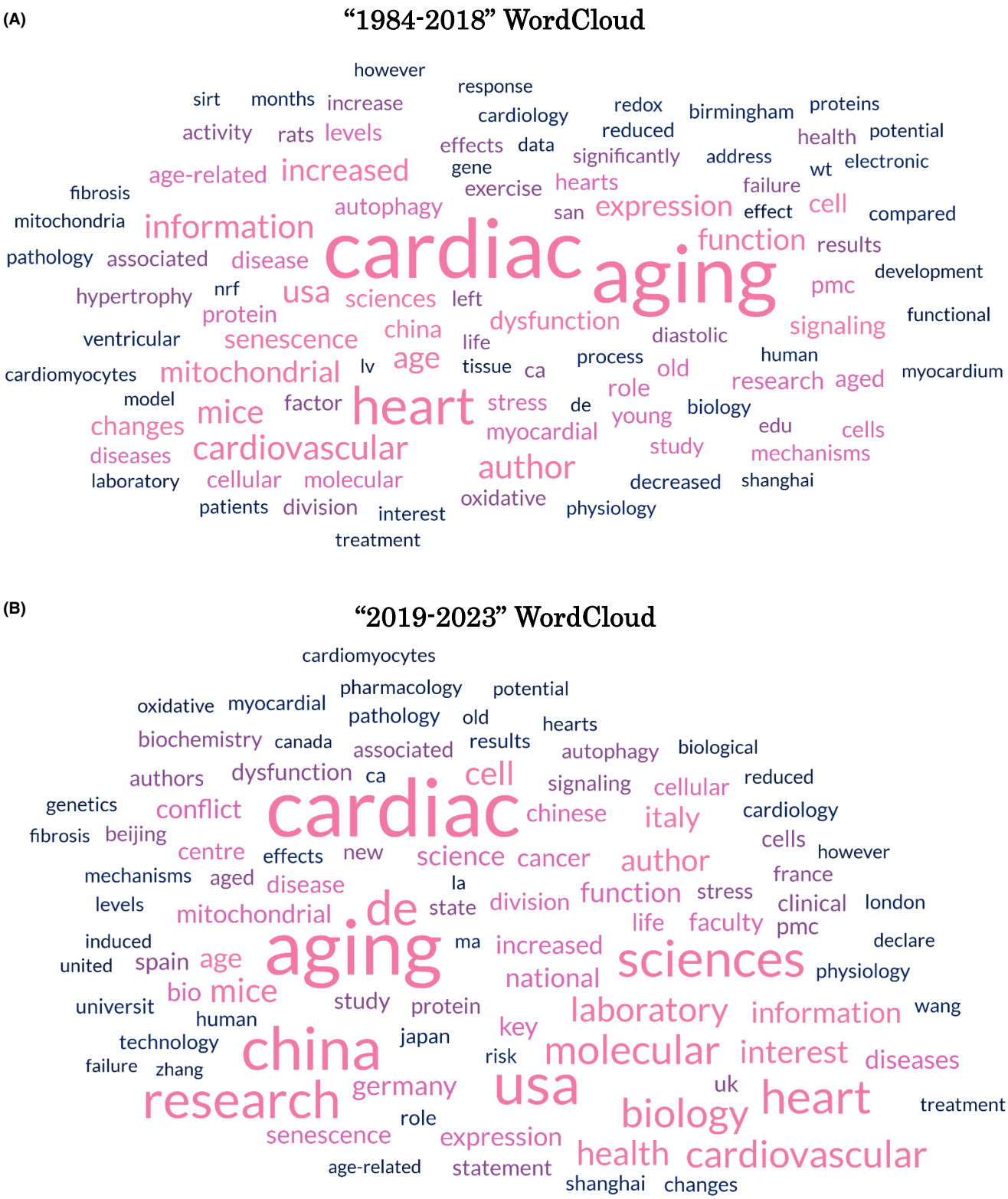

FIGURE 3 As the bubble plots differed between 1984–2018 and 2019–2023 in Figure 2B, especially for the term "mitophagy," which showed a significant increase in the number of occurrence, we created word clouds for each period, divided into "1984–2018" (A) and "2019–2023" (B). We used Free Word Cloud Generator (FreeWordCloudGenerator.com) to create word clouds of all PubMed articles from 1984 to 2018 (A) and those from 2019 to 2023 (B).

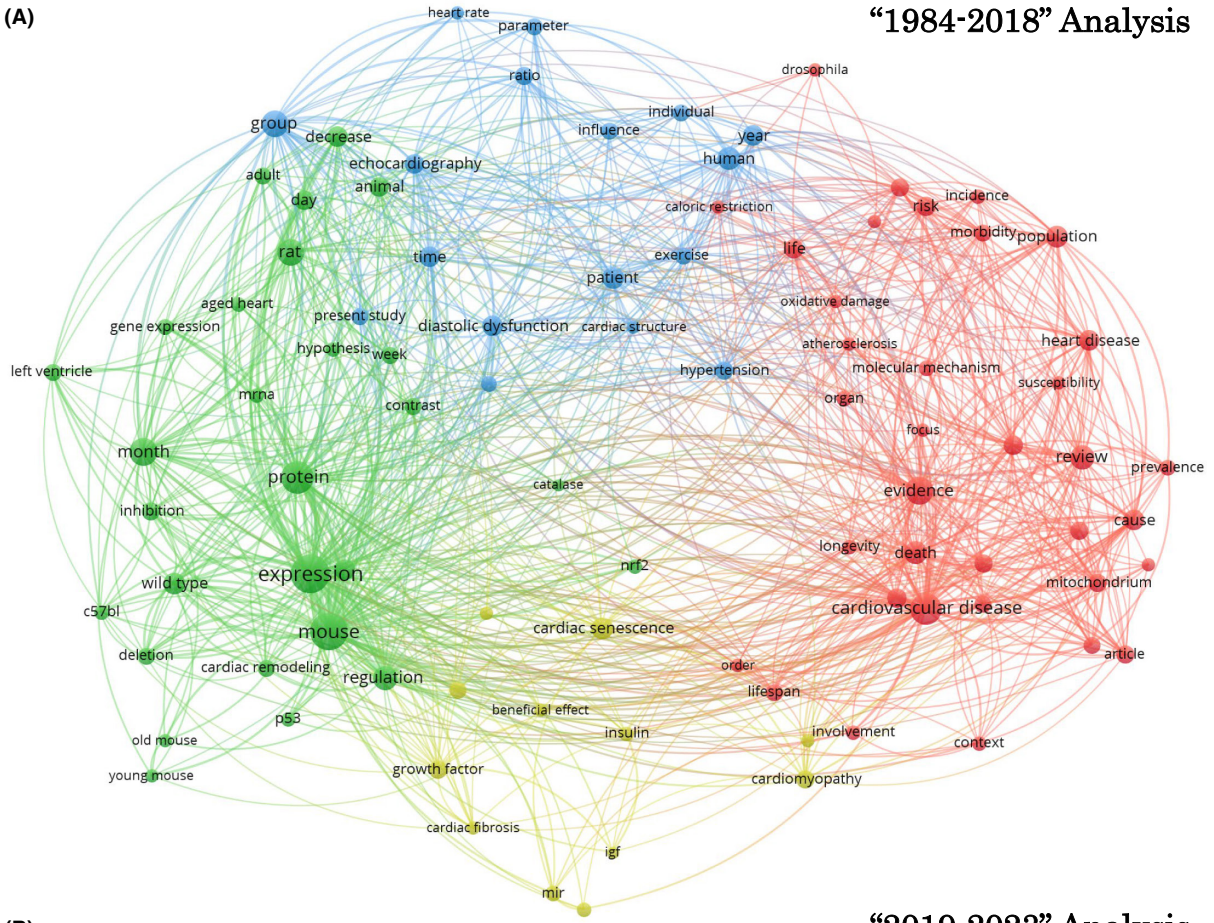
(A)
"1984-2018" Analysis
heart rate
parameter
ratio
drosophila
individual
influence
year
human
group
decrease
echocardiography
adult
animal
day
rat
time
exercise
patient
caloric restriction
risk
incidence
morbidity
population
life
aged heart
present study
gene expression
diastolic dysfunction
cardiac structure
oxidative damage
hypothesis
week
atherosclerosis
heart disease
left ventricle
hypertension
molecular mechanism
susceptibility
mrna
contrast
organ
focus
month
protein
catalase
review
prevalence
evidence
inhibition
cause
longevity
death
nrf2
wild type
expression
mitochondrium
c57bl
cardiovascular disease
mouse
cardiac senescence
deletion
cardiac remodeling
regulation
order
article
lifespan
p53
beneficial effect
insulin
involvement
context
old mouse
young mouse
growth factor
cardiomyopathy
cardiac fibrosis
igf
mir
(B)
"2019-2023" Analysis
presence
death
cardiac disease
mitochondrial function
cause
review
mitochondrial dysfunction
ros
major risk factor
understanding
production
loss
parkin
mitophagy
population
type
disease
impairment
p53
protein expression
heart function
lifespan
patient
cardiomyocyte
prevalence
year
human
present study
old mouse
cvd
senescence
cardiovascular disease
risk
oxidative stress
cellular senescence
cardiomyopathy
left ventricle
incidence
research
cardiac senescence
mortality
risk factor
dox
activity
model
life
sex
d gal
vitro
stress
important role
apoptosis
expression
echocardiography
month
animal
animal model
marker
hypertension
rat
group
atherosclerosis
female
week
myocardial infarction
cardiac fibrosis
extracellular matrix
tef

FIGURE 4 Similar to Figure 3, as the bubble plots in Figure 2B differed between 1984–2018 and 2019–2023, we constructed bibliometric networks for studies conducted in "1984–2018" (A) and "2019–2023" (B) via VOS viewer 1.6.20. Compared with (A, B) showed an increase in the number of terms indicated in red circles which are related to the mechanisms of cardiac aging such as "mitochondrial dysfunction," "mitophagy," "parkin," "apoptosis" and "p53."

4 | DISCUSSION

Review articles on cardiac aging are abundant, but they may not provide an objective evaluation of the studies. It can be challenging to assess cardiac aging studies solely based on review papers. This study used text mining[17] to extract essential information on cardiac aging from a large amount of text obtained from all accessible studies on PubMed to date. Although AI has made remarkable progress in recent years, popular AI tools, such as ChatGPT and BARD, cannot process the large amount of text extracted in this study (as of November 30, 2023). Therefore, text mining, such as that used in this study, remains the standard tool for research purposes when using a large amount of text.

4.1 | Frequently used terms in cardiac aging research

The most frequently used adjectives included "mitochondrial," "oxidative," "diastolic," "inflammatory," and "diastolic." Other terms were "mouse," "human," and "model," which indicate the research subjects. We also created a list of the most frequently used nouns, with "cardiomyocyte," "autophagy," "hypertrophy," "fibrosis," "apoptosis," "mitochondrium," "damage," "mitophagy," and "inflammation" appearing frequently. KH Coder also refers to the corresponding parts of the sentence where the term appears. Although the term "damage" was nonspecific, it was frequently used as "DNA damage" and "protein damage" in the text. Regarding cardiac aging, there were several references to diastolic function, hypertrophy, fibrosis, and apoptosis, which were frequently mentioned as tissue types. Moreover, there were several references to mitochondria. Additionally, mechanisms such as oxidative stress, autophagy, mitophagy, and damage (DNA damage or protein damage) were mentioned (Figure S2). In terms of cell types, the majority of references are to cardiomyocytes.

4.2 | Multifaceted evaluation using text mining tools

An appeal of text mining is that it can be used to extract terms that are used simultaneously with figures (Figure 1C). Using several text mining tools, we extracted terms that may have important roles by creating various figures (Figure 1A–D). As tissue changes, fibrosis, hypertrophy, and apoptosis commonly appear in several figures, while oxidative stress, autophagy, mitophagy, and damage (DNA damage or protein damage), which may be mechanisms of these changes, also appear frequently (Figure 1A,B). Although KH Coder and Word Cloud Generator primarily focused on these terms, analysis via VOS viewer showed that diastolic dysfunction, blood pressure, and atrial fibrillation were grouped in blue, which means outstanding (Figure 1D). This may be due to the specificity of VOS viewer, which constructs and visualizes bibliometric networks formed by relationships between academic studies and authors. By using VOS viewer in this study, we obtained results that could not be obtained with KH Coder or Word Cloud Generator alone. Additionally, VOS viewer enabled the extraction of characteristic genes, such as p53 and p16, in a group that was colored yellow and centered on the term "senescence." p53 and p16 are essential genes when discussing oxidative stress and DNA damage, and they are considered indispensable genes when discussing cardiac aging.[18,19]

4.3 | Evaluation of the extracted terms

A self-organizing map was constructed by extracting terms that appeared to be specific based on the abovementioned analysis (Figure 2A). The terms "ventricular" and "atrial" were located in the lower left and lower right parts, respectively, and separated by several boundaries, suggesting that they are being used distinctively in research. We also found that the term "atrial" is often used with the terms "lesions," "cardiomyocyte," and "tissue"; this confirmed that atrial aging is being discussed in the literature. Additionally, the term "atrial" is often used as "atrial fibrillation," suggesting that atrial fibrillation is one of the diseases being discussed together with cardiac aging. Meanwhile, the terms "mitophagy," "mitochondria," "apoptosis," "autophagy," "inflammation," and "ROS" were likely concentrated in the right upper part, indicating that these phenomena are frequently used in the same context. We then assessed the bubble plot (Figure 2B), which suggested that research on the atrium is more advanced than that on the ventricle; it further indicated the frequency of occurrence of "autophagy" is increasing. Moreover, we revealed an increase in the frequency of occurrence of terms related to "mitophagy," "mitochondria," "apoptosis," "autophagy," "inflammation," and "ROS", suggesting that autophagy research has made a breakthrough in the field of cardiac aging, and the related mechanisms have been clarified. We conducted a study that followed the current trend of frequent discussion on the relationship between autophagy and cardiac aging.[20] Even in case of atrial fibrillation, our previous research revealed that atrial fibrillation is related to autophagy.[21] It was also elucidated that the frequency of occurrence of "mitophagy" increased significantly since 2019. When we compared the word clouds created for "1984–2018" and "2019–2023" (Figure 3A,B), the term "mitochondria" appeared frequently until 2008, and the term "autophagy" appeared frequently since 2018.

This suggests that cardiac aging may be due to an abnormality in mitochondria; however, it is believed that the mechanisms involve an abnormality in autophagy, especially mitophagy. In fact, VOS viewer revealed a red cluster centered on the terms "mitochondria" and "mitophagy" in the analysis of "2019–2023" (Figure 4B).

4.4 | Important terms determined via machine learning

We trained NCBI's LitSuggest using literature from "1984 to 2018." We then extracted literature published in the past 5 years ("2019–2023") that followed the trend of previous research on cardiac aging. From the 10 studies that AI excluded, the word cloud showed nonspecific terms (Figure S3). Meanwhile, 261 of 271 studies were closely related to previous research on "cardiac aging." The word cloud created from these 261 studies (Figure 5A) showed specific terms such as "mitochondrial." The protein "parkin," which is necessary during mitophagy, also appeared frequently.[22] Parkin, which is a product of a Parkinson's disease-causing gene, plays an important role in regulating mitophagy. Normal parkin control is lost with aging, and research is being conducted on the relationship between parkin and mitochondria, which is related to both cell survival and cell death.[23,24] Additionally, "nrf2," which is important in oxidative stress, also appeared in the word cloud. The KEAP1-NRF2 regulatory system is a biological defense mechanism that responds to foreign substances and oxidative stress. As oxidative stress mainly occurs in mitochondria, the KEAP1-NRF2 regulatory system is

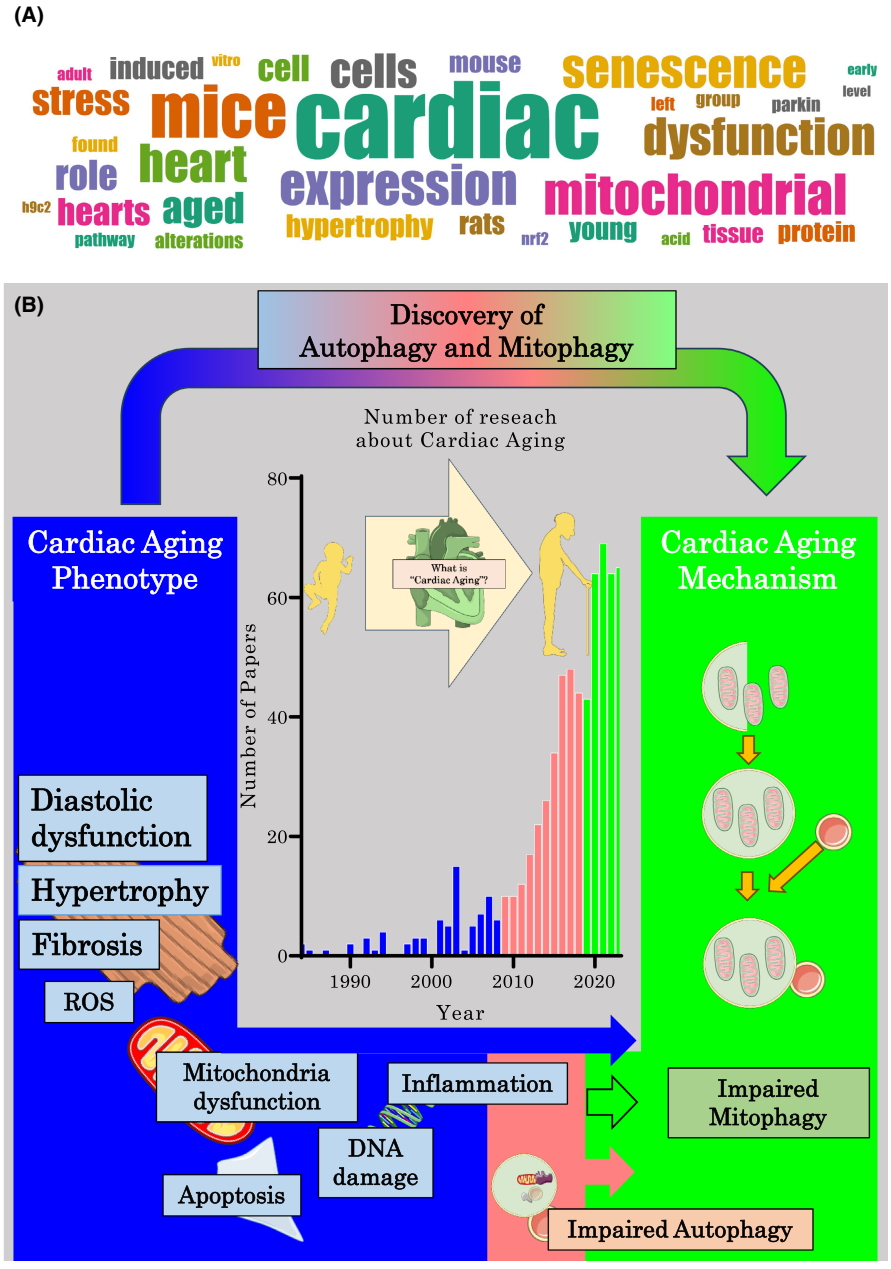

FIGURE 5 (A) After training LitSuggest on studies conducted from 1984 to 2018, we created a word cloud from the 261 studies that were extracted from the 5-year period of 2019–2023 and were closely related to previous research on cardiac aging. LitSuggest was developed by the National Center for Biotechnology Information. The term "mitochondrial" stands out, and the terms "parkin," which is related to autophagy, and "nrf2," a gene related to redox, were also observed. (B) This figure summarizes the findings of the study. Previously, cardiac aging was often described in terms of cardiac dysfunction and tissue phenotypes such as diastolic failure, cardiac hypertrophy, and fibrosis. However, with the discovery of autophagy and mitophagy and advancements in their research, cardiac aging is currently described in terms of its underlying mechanisms. Parts of the figure were constructed using pictures from Servier Medical Art. Servier Medical Art by Servier is licensed under a Creative Commons Attribution 3.0 Unported License (https://creativecommons.org/licenses/by/3.0/). ROS, reactive oxygen species.

thought to control mitochondrial function through oxidative stress control.[25,26] However, reports have revealed that the KEAP1-NRF2 regulatory system can also directly control mitochondrial function.[27] This study objectively demonstrates that there is active discussion in the literature regarding cardiac aging, redox reactions, and mitochondrial function while focusing on mitophagy.

4.5 | What is cardiac aging?

Cardiac aging is a concept frequently discussed in terms of cardiac function and histological changes, such as "diastolic dysfunction," "hypertrophy" of cardiomyocytes, "fibrosis," and induction of "oxidative stress." Meanwhile, there has been progress in the research on more fundamental causes of cardiac aging, such as "mitochondrial dysfunction," "apoptosis," "DNA damage," and "inflammation." In addition to the increasing discussion on "autophagy," discussion regarding cardiac aging has become more active, and the number of publications on this condition has increased. Currently, "mitophagy" is a topic that has gained widespread attention in cardiac aging research (Figure 5B). This suggests that proposals regarding cardiac aging are also shifting from tissue or functional mechanisms to more fundamental ones, i.e., the progression of "mitophagy" impairment in cardiac aging.

4.6 | Autophagy and mitophagy

An increasing number of studies have suggested that autophagy, especially mitophagy, plays an important role in cardiac aging. Autophagy is a biological phenomenon wherein a cell breaks down its parts, and the phenomenon that selectively breaks down mitochondria is known as mitophagy; these processes play vital roles in the heart, an organ that does not regenerate. This study also revealed that the relationship between autophagy and cardiac aging was first proposed in 2009,[28,29] and the number of studies on autophagy and cardiac aging has increased in the past 5 years. Since the publication of a review on cardiac aging, autophagy, and mitophagy in 2016 by Shirakabe et al.,[30] the number of studies on these topics has increased. Although myocyte hypertrophy, fibrosis, and increased oxidative stress occur during cardiac aging, the discovery of autophagy and mitophagy and advancements in their research have led to a significant increase in the number of studies on cardiac aging.

The preeminent role of mitochondria within cardiomyocytes cannot be overstated, given that mitochondria constitute approximately one-third of the cardiomyocyte volume. The processes of mitophagy, along with other mitochondrial functions, are crucial within the myocardium; a tissue characterized by its substantial energy demands. Furthermore, a portion of the oxidative stress encountered in this context is mediated through the mitochondrial membrane, underscoring the significance of mitochondrial integrity in cardiomyocyte function. The centrality of mitochondria in research concerning cardiac muscle tissue is incontrovertible. This study definitively establishes that the elucidation of autophagy precipitated the identification of mitophagy, thereby significantly enhancing our understanding of mitochondrial dynamics in cardiac muscle. Moreover, the exploration of mitochondria's clinical applications is currently underway, suggesting that the discovery of mitophagy might well be heralded by future scholars as pivotal advancement in unraveling the complexities of "cardiac aging."

4.7 | Limitations

There are mainly three limitations.

First of all, the limitation of this study is that although text mining can analyze text, it cannot understand its meaning. Text mining simply recognizes the number and types of terms used in the text and analyzes the specific features of the text. As machines do not understand text, we evaluated each term based on the original text in this study; however, it is difficult to indicate whether a process is being performed objectively and neutrally.

Secondly, an inherent constraint of employing text mining and machine learning methodologies lies in the interpretation of figures and outcomes, which remains susceptible to the subjective lens of the interpreter. This susceptibility suggests that a deficiency in domain-specific knowledge may precipitate a misinterpretation of the results of the inadvertent introduction of bias, notwithstanding a comprehensive analysis of the extant literature. To mitigate this concern, we have instituted measures aimed at refining the accuracy of our interpretative process. This involved the inclusion of a cadre of geriatricians and cardiologists within the framework of this study, thus leveraging their specialized expertise. Furthermore, to safeguard against potential biases and ensure impartiality, we solicited the insights of a physician affiliated with another prominent clinical institution.

Thirdly, it is pertinent to acknowledge a limitation of this study stemming from its exclusive focus on English-language research, potentially overlooking significant contributions in other languages, notably Japanese and Chinese. This linguistic constraint may inadvertently exclude pioneering studies, particularly those emanating from China, where there is a rich tradition of research in areas such as traditional Chinese medicine, often disseminated primarily in the native language. Confining this study to the English language may have constrained its diversity, potentially restricting its exploration within a wider academic panorama and limiting the scope of text mining to research predominantly engaged with on a global scale. Despite these constraints, we recognize the inherent challenges in surmounting such limitations. However, it is our conviction that the advancing trajectory of large language models heralds a future of increased versatility for this methodology, as these models evolve to proficiently encompass a broader linguistic spectrum.

5 | CONCLUSION

This study visualized "what cardiac aging is" through text mining. In the context of bodily tissues, cardiac aging is characterized by

hypertrophy, fibrosis, apoptosis, and increased oxidative stress. However, the mechanisms underlying cardiac aging may include impairment of autophagy, especially mitophagy. We expect that the mechanisms of cardiac aging will be clarified further in the future. Thus, this study revealed the overall understanding of cardiac aging among researchers.

AUTHOR CONTRIBUTIONS

T.K. conceived and designed the study, collected, and reviewed all data, and wrote the initial draft of the manuscript. K.T. was part of the preparations and contributed the discussion, especially in data science. T.O. contributed to the discussion, especially in Aging medicine as Geriatrics Specialist. S.K. verified the discussion was not biased. A.H., M.K., and A.S. reviewed all data and contributed to the discussion, especially in the cardiovascular field.

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CONFLICT OF INTEREST STATEMENT

The authors declare that there are no conflicts of interest.

DATA AVAILABILITY STATEMENT

All data generated or analyzed during this study are included in this article and supporting information. Further inquiries can be directed to the corresponding author.

ETHICS STATEMENT

This text mining analysis did not require approval from the ethics committee of National Center for Geriatrics and Gerontology because this study did not include any studies with human participants or animals.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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