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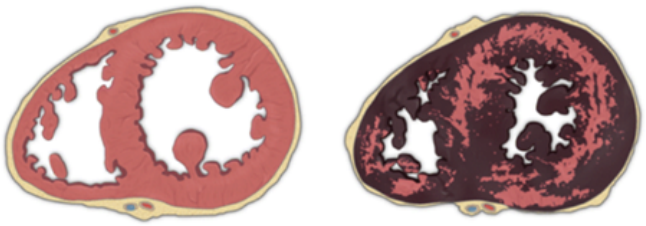
To understand a rare disease

------ The Cardiac Amyloidosis

1. Introduction

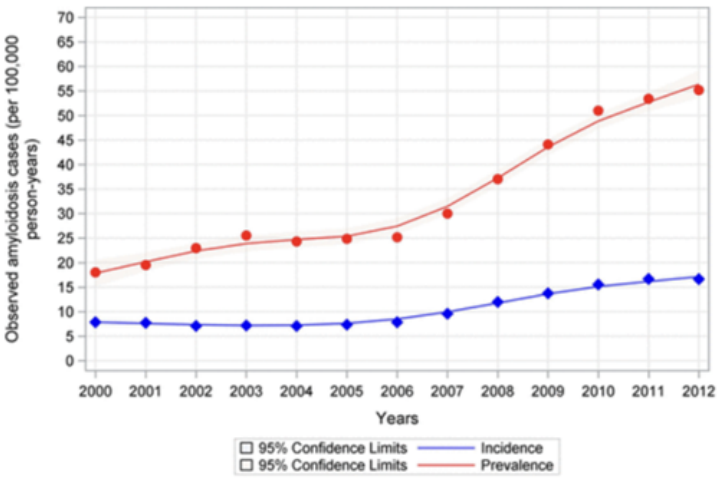
There are numerous diseases in our surroundings. Thanks to advancements in medical technology, doctors can now rapidly diagnose disease symptoms and provide effective treatment for patients. However, there are also rare diseases, such as cardiac amyloidosis. Due to its rare occurrence, this disease gained attention in China in 2015. What's more, due to a lack of understanding about this disease, cardiac amyloidosis is often misdiagnosed. Cardiac amyloidosis, just like its name implies, occurs because of the deposition of abnormal proteins in tissues of the heart. To be more specific, *Transthyretin amyloid (*ATTR) caused by a protein called transthyretin (TTR), shapes its shape and then turns into clumps Al are two subtypes of cardiac amyloidosis. For the first subtype, this happens with related genes or family history. That means if individuals have this disease, their children will also develop cardiac amyloidosis, as it typically occurs between the ages of sixty and seventy. Therefore, age is also a cause of cardiac amyloidosis. On the other hand, Al is susceptible to certain cancers, such as bone cancer. Besides, there is only about a 2 percent probability related to inflammations. Inflammation could impair their functions, resulting in a decrease in the pumping ability of blood or negatively affecting our signal transmissions. Besides impacts on hearts, cardiac amyloidosis would also damage other organs, such as the liver, brain nerves, and kidneys. The prognosis for cardiac amyloidosis in the population is poor.



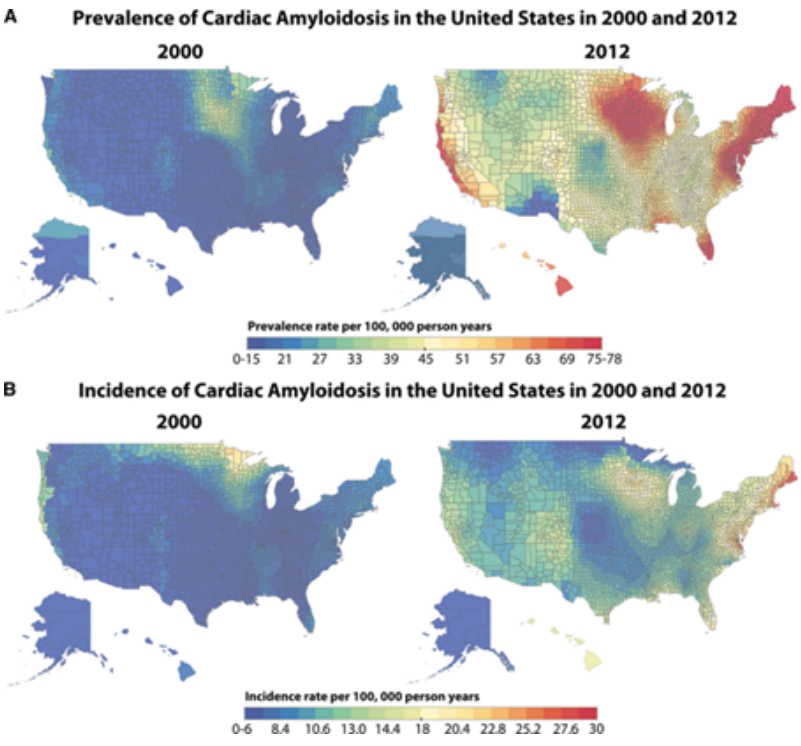
Normal heart　　Cardiac amyloidosis

2. Current trend

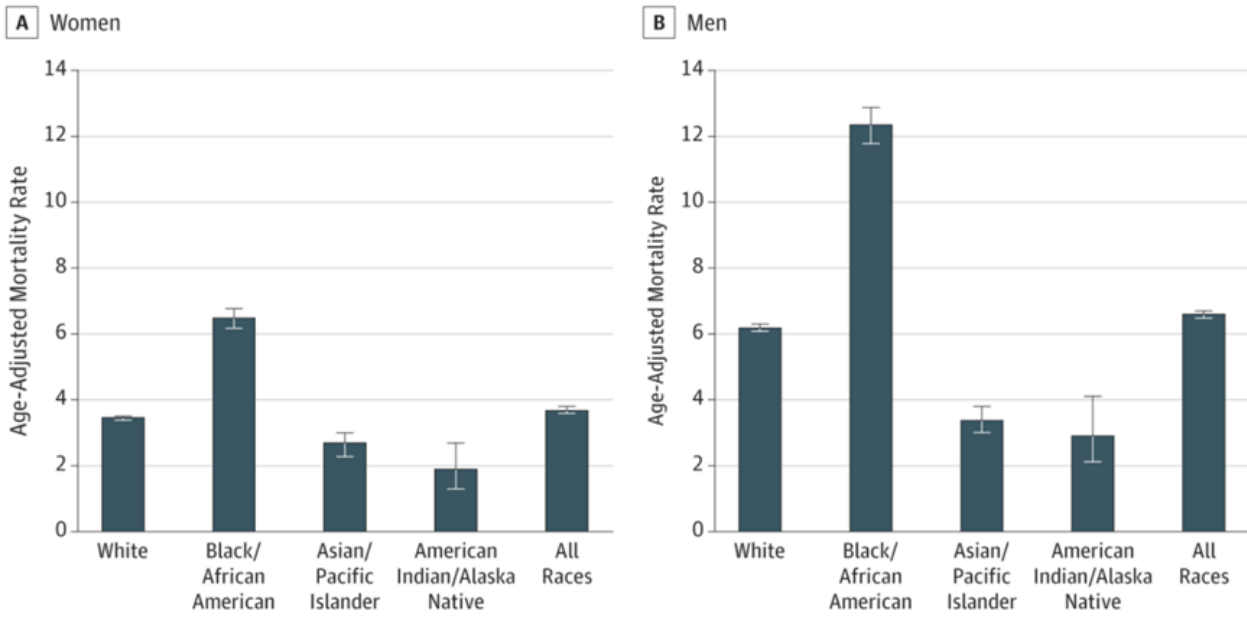
Medical professionals can more accurately diagnose patients with cardiac amyloidosis. Thanks to advanced technology in medical equipment. And there are fewer cases of this kind of disease being missed. Cardiac amyloidosis is a condition that is spreading worldwide and gaining more recognition. The study found an increase in the incidence of cardiac amyloidosis, from 18.0 per 100,000 people per year to 55.2 per 100,000 people per year. The most common reason was that large amounts of underdiagnosed cardiac amyloidosis were being identified. Because of the similarity of AL, which is called amyloidosis light chain, with Hodgkin's lymphoma or chronic myelogenous leukemia. The probability of a missed diagnosis is very high. Advanced technology, such as cardiac imaging, contributes a lot of effort to identifying cardiac amyloidosis.



From the graph above, we can analysis that there was a turning point roughly in 2006, and later a huge increase between 2006 and 2012. Taking getting cardiac amyloidosis in the United States as an example, in different regions of the United States, there is a huge difference in getting cardiac amyloidosis. According to statistics on cardiac amyloidosis



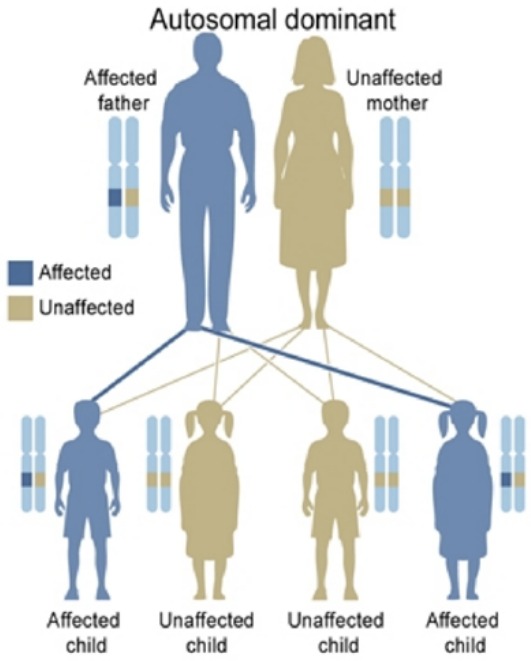
prevalence, the states of California, Florida, Hawaii, the east, and the northeast of the United States have the highest rates of the disease. Additionally, Maine and the East Coast of the United States have the highest rates of cardiac amyloidosis, which are correlated with the prevalence of the disease. If black Americans have the highest rate of cardiac amyloidosis based on race, they are more likely to get this disease. Especially in hereditary transthyretin amyloid, which is one of the types of cardiac amyloidosis.



This type of amyloidosis has a close connection with genes. Cardiac amyloidosis is caused by a transthyretin gene, which is very rare in humans. However, it is common among black Americans. According to the research, it shows that these people carry a gene that enables them to be more sensitive to salt than others. Therefore, black Americans are more likely to get high blood pressure and heart disease. What's more, studies show that the most common age at which people get cardiac amyloidosis is over 50 years, and it is very rare that a person gets it in the early 20s. Moreover, cardiac amyloidosis happens more commonly among men than women. 25 to 50, in ATTR amyloidosis in particular.

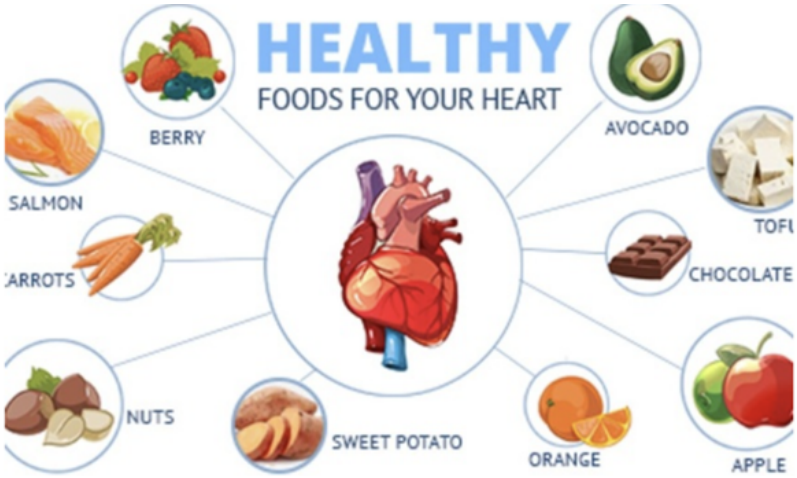
3. Etiology

There are two types of cardiac amyloidosis, light chain (AL) and transthyretin amyloidosis (ATTR), as I already mentioned. The immune system is to blame for it happening to the light chain. The immune system is generally necessary for maintaining human health. However, some immune diseases, such as Tuberculosis Sjogren's syndrome, and rheumatoid arthritis, would enable immune cells to be inactive and not work anymore. After that, amyloid deposits begin to form in additional organs, and cardiac amyloidosis is the result later. Most of AL sufferers are typically between the ages of 50 and 60. The causes of ATTR cardiac amyloidosis can be divided into two categories. The first is a hereditary trait, and the second is a wild type. TTR is the amyloid precursor protein that can lead to the deposition of amyloid. The liver also produces all TTR. If a person is born with a mutated TTR gene, his family will probably have ATTR as well. From the figure, we know that ATTR is an autosomal dominant inheritance. The man has a mutated chromosome and a normal chromosome, and the woman has a normal gene. After calculating, we know each of their children has a half chance of getting ATTR. From the perspective of gender, male children have an equal chance compared with female children. Both have a fifty percent probability of receiving transthyretin amyloidosis. Instead of being passed down through families, wild-type TTR (wt TTR) results from the protein misfolding itself. This



happens as people age because abnormal amyloid substances gradually build up in cardiac muscle cells. This damages the muscles over time, making them less able to pump blood. Finally, it induces cardiac amyloidosis.

Even though diets will not cause cardiac amyloidosis. A healthy diet, however, can lower your risk of contracting this illness. The burden on the heart, such as cardiovascular disease (CVD) brought on by the accumulation of fatty plaques, is typically increased by high cholesterol and a high-fat diet. The kidney acts as a cleaner in our body because it can remove waste. If the kidney is damaged, it will affect the heart indirectly through high blood pressure. Therefore, people need to remember not to eat too much protein in a day. Except for proteins and saturated fats, people with cardiac amyloidosis need to reduce their sodium intake as well. Recommended amounts of sodium intake are less than 1500 mg each day. People can choose apples and cherries because these fruits can reduce the risk of heart disease and contain vitamins A and C.



Consuming less sugar is also crucial. Avoid any beverages that contain sugar. Water with lemon is the best beverage for people with cardiac amyloidosis. Desserts should also be avoided because they lack vitamins, fiber, and minerals, which are good for your health.

There is no denying that exercise can improve people's health. However, patients with cardiac amyloidosis should first discuss this with their doctors before developing a plan for exercising. Some light exercises are suitable for those with cardiac amyloidosis, such as walking, jogging, and cycling. Because these exercises can help them reduce their blood pressure, heart rate, and kidney failure. On the other hand, intense exercise not only does them little good but also makes their conditions worse.

4. Diagnosis and Treatment

Nicolaus Fontanus discovered the first instance of amyloid disease in 1639. In 1838, Matthias Scheiden gave amyloidosis a name. When he added iodine to the sample, the color changed to a blue that resembled starch. Cardiac amyloidosis is difficult to diagnose due to its lack of specificity. As a result, people with cardiac amyloidosis are often misdiagnosed. Today, medical technology is becoming more developed. Six techniques exist for identifying if an individual has cardiac amyloidosis, such as urine tests, blood tests, an MRI of the heart, an ECG or EKG, an echocardiogram, and a biopsy. A biopsy is thought to be the most effective and precise method for identifying cardiac amyloidosis. When performing a biopsy, a tiny piece of skin is removed from either the bone marrow or the abdomen. After obtaining this small sample, doctors will use a microscope to analyze what kind of amyloid is contained in people. To examine blood, doctors often use a dye called Congo-red stain. The patient has amyloidosis if the sample's color changes to green. This is one type of biopsy called a tissue biopsy. Another one is called an organ biopsy. If the result of the tissue biopsy is negative, but doctors still cannot confirm it, then patients will undergo a surgical biopsy, which requires taking a sample from the liver, stomach, or intestines. If the sample's outcome is positive, a light chain can be verified. The presence of AL can also be determined by doctors using bone marrow aspirates and biopsies.

There is no way to cure cardiac amyloidosis properly. However, some medications can help patients lessen the effects of cardiac amyloidosis and stop the production of new proteins. When treating cardiac amyloidosis, hospitals often allow different experts to work together to come up with a proper plan for patients. Hematologists, cardiologists, gastroenterologists, pulmonologists, nephrologists, and neurologists are usually members of the team. They will collaborate to consider the adverse effects of conservative medicine or surgery. Medicines include RAAS inhibitors such as Furosemide and captopril, which can be used for patients in the treatment of heart failure, and Magfaran and dexamethasone, which can reduce the production of proteins. A difficult surgery because it is challenging to match the heart is called combined heart and liver transplantation (CHLT). It can be used to treat inherited cardiac amyloidosis, but so far only a handful of cases have been documented globally. There is still more to learn about treating cardiac amyloidosis. The UT Southwestern Medical Center has recently conducted additional clinical studies to investigate more potential new medications.

5. Conclusion

Acquiring knowledge of and understanding of such a rare disorder as cardiac amyloidosis is imperative. Although the possibility that a person will get this disease is low compared with other diseases. Unfortunately, the amount of people affected by cardiac amyloidosis is going up because of bad habits like drinking, eating unhealthy food, and leading a sedentary lifestyle. Moreover, this disease cannot be cured completely. But, in the past five years, scientists and researchers have made huge progress in dealing with cardiac amyloidosis. Joban Vaishnav, who is a cardiologist at the Johns Hopkins Comprehensive Center, developed a new medication called tafamidis, which can treat cardiac amyloidosis, and was approved to be applied to patients in 2018. To better treat people who get this disease, in that center, there is a team that will develop medications and provide clinical trials to deal with cardiac amyloidosis. While medications are very expensive and not many patients can afford them. Johns Hopkins' specialty pharmacy provides many drugs for those patients, which gives them hope because

they do not have to worry about such huge expenditures on medications. Besides, CRISPR technology is widely used in treating diseases. Even though there are not many CRISPRs that are applied to cardiac disease. However, studies showed that in experiments with mouse hearts, researchers found that after deleting the relevant gene in the DNA of mouse heart muscle cells using CRISPR technology, mice's hearts could be restored. Afterward, experiments applied to mammals such as macaques have shown promise in the treatment of human cardiovascular disease with CRISPR technology. Therefore, we can think about whether the CRISPR technology can be applied to treat cardiac amyloidosis by cutting a gene that can mutate the protein to be ATTR amyloidosis.

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