The Comparison and Contrast on NAFLD between the East and the West: Metabolic Mechanism, Dietary Habits, and Policies

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Abstract. As non-alcoholic fatty liver disease (NAFLD) is becoming prevailing in both western and eastern countries, it affects people's liver health and causing more severe diseases such as cancer, cardiovascular diseases, and type II diabetes worldwide. In this case, exploring NAFLD itself further and studying the difference between western and eastern countries from various perspectives is important for decreasing NAFLD cases. In this article, we aimed to investigate the metabolic mechanism of NAFLD, how the difference in dietary habits influenced the incidence of NAFLD worldwide, and the similarities and disparities between NAFLD policies from the East and those from the West. To reach this goal, we reviewed literature in English and Chinese that discussed NAFLD and non-alcoholic steatohepatitis (NASH) and visited official websites related to liver health. As a result, we concluded that most of the drugs designed based on fatty acid sources and metabolism had deficiencies, and lifestyle change was the best treatment. Western countries consume more meat, fewer vegetables, and a relatively similar number of fruits as eastern countries. The East and the West have relatively similar incidences of NAFLD. The high consumption of olive oil, vegetables, fruits, and whole grains and a low intake of meat in the Mediterranean diet led to a lower incidence of NAFLD in the Mediterranean area than in other places. There was overall a lack of policies on NAFLD. Still, while exploring the ones we currently had, there were some agreements and disagreements on NAFLD policies about lifestyle, diagnosis, treatment, research, organization, social problems, patient-centered care, and coalition between western and eastern countries. There were also diverse suggestions and different potential suggestions from these perspectives between the East and the West.

1 Introduction

To explore the mechanism of NAFLD and compare and contrast the dietary habits and policies between the East and the West, we reviewed English and Chinese literature about NAFLD and NASH. We visited official websites related to liver health to collect information about mechanisms, dietary habits, and policies [1]. In particular, for the mechanism part, we are going to illustrate: the influence of NAFLD both on the liver and extra-hepatic organs[2], the sources of fatty acid and treatments based on these sources, the metabolic process of fatty acid and corresponding treatments, factors that cause NAFLD patients’ death, different treatments of NAFLD and NASH based on metabolism and their disadvantages, and why keeping a healthy lifestyle is the best way to treat NAFLD[3,4]. To discuss dietary habits in-depth, we are going to talk about: the comparison of the consumption of meat, vegetables, and fruits and the NAFLD incidence between the East and the West, what Mediterranean diet is and why it is healthy, what Mediterranean diet is rich in and what it only contains little, the low NAFLD incidence in Mediterranean region, and the current dietary trend among people. For policies, we are going to talk about: the general lack of policies on NAFLD, policies about lifestyle change on diet and physical activities, policies about improving diagnostic methods and tools, policies about who should receive pharmacological treatment, policies about doing more research on MS (metabolic risk factors) and hepatitis B virus (HBV), policies about forming organizations to improve people’s liver health, and policies that are concerned with social problems, patient-centered care, and coalition.

2 Metabolism of NAFLD

NAFLD is a multisystem disease that affects liver health and extra-hepatic organs and regulatory pathways. For example, NAFLD increases the risk of type 2 diabetes (T2DM), cardiovascular disease (CVD), and heart disease, and chronic kidney disease (CKD), which is the leading cause of death in NAFLD patients [5].

Over the past three decades, non-alcoholic fatty liver disease (NAFLD) has evolved into the world’s most common cause of chronic liver disease [6]. Studies have...
shown that 25% of the world's population is now thought to have non-alcoholic fatty liver disease [7]. Nonalcoholic steatohepatitis (NASH) is a subtype of NAFLD that can progress to hepatocellular carcinoma (HCC) with cirrhosis and death. NAFLD and NASH occur not only in adults but also in children and adolescents [8]. Because NAFLD is closely associated with type 2 diabetes (T2DM) and obesity, models predict that the prevalence of NAFLD and NASH will increase, which will cause several social problems. However, there is no accurate non-invasive method to detect Nash. The mechanisms are not yet understood, and therapeutic targets are still in the process of being studied, so the treatment of this disease is limited to lifestyle changes [9].

When we talk about the mechanism and treatment of NAFLD, we usually break it down into two parts: where does the fatty acid in the liver come from, and how does it metabolize.

Fatty acids are transported from the blood to the liver primarily through the lysis of triglycerides in adipose tissue, a process that is regulated by insulin on adipocytes [10]. The second major source of fatty acids is glucose and fructose via de novo lipogenesis (DNL). Studies have shown that increased lipid content in the liver of patients with NAFLD is mainly due to DNL [11]. DNL can be pharmacologically inhibited by targeting its synthases [12].

Fatty acids and carbohydrates from the liver to other organizations, such as peripheral adipose tissue, brown adipose tissue, and skeletal muscle, also reduce their liver accumulation. Peroxidase body growth, such as activated receptor gamma (PPAR) ligand, a special type of nuclear receptor ligands, fat cells store fat and improve the NASH. However, the cost increases peripheral fat stores and weight gain [13]. The depletion of these energy donors in the muscle tissue and brown adipose tissue involved in exercise also promotes their transfer to extrahepatic tissue. Thus, one proposed treatment strategy for the prevention or treatment of NASH is to increase the abundance and function of brown adipose tissue [14]. Fatty acids in the liver are non-covalently bound to fatty acid binding protein-1 (FABP-1, also known as liver type FABP (L-FABP)), mainly through mitochondrial oxidation or esterification metabolism to form triglycerides [15].

Processing of fatty acids by forming triglycerides is generally considered an adaptive protective response to an excess of fatty acid supply in metabolic capacity [16]. But studies have shown that superfluous triglyceride can also cause metabolic abnormalities [17]. Triglycerides in the liver are not directly transported into the bloodstream because very low-density lipoprotein (VLDL) forms lipid droplets in liver cells, a defining feature of NAFLD. These droplets may form intracellular pools of fatty acids after fat breakdown [6].

In recent years, changes in diet, livestock, and the widespread use of antibiotics in humans have altered the human microbiome, which is also thought to be one cause of increased NAFLD populations [18]. People began to find that change of microbial groups and possible mechanism of the relationship between the fatty liver, and through the intestinal FXR signal and the release of fibroblast growth factor 19 regulate bowel liver shaft intestinal bacterial activity (FGF19), regulating bile acid synthesis. In addition, the change of lipid and glucose metabolism microbial groups (disorder) could also lead to increased intestinal permeability, amplifying many of these derivative effects in the gut [19].

Accumulation of extracellular matrix in liver results in progressive fibrosis of liver cirrhosis portal hypertension, and liver failure is the leading cause of death in patients with NAFLD liver related. Fiber is generated by stress or injury of liver cells and activated macrophages (Kupffer cells) in the liver signal of driven, leading to the hepatic stellate cells activation of muscle fiber cells, to produce less than the speed of degradation of faster matrix proteins [20].

**3 The influence of dietary habits on NAFLD**

The Mediterranean diet represents the traditional diet of the Mediterranean sea countries, like Spain, France, and Italy. The characterization of this diet is to consuming abundant vegetables, fruits, beans, cereals, and seafood with a large amount of olive oil. It restricts the consumption of meat and alcohol [7, 21]. Mediterranean diet is a macronutrient diet that is beneficial to the metabolic system, especially lipidic metabolism. This diet is derived from the special environment, and studies have shown that the Mediterranean diet is healthier than other diets. NAFLD is a highly prevalent disease globally the world. The Mediterranean area has a lower prevalence rate than other areas.

People who follow the Mediterranean diet have healthier bodies than people who follow other diets. The prevalence of total cardiovascular or cancer mortality is significantly lower in the Mediterranean diet [7]. Besides, in the age 70 – 90 European group, there is about 23% lower all-causes death who adhere Mediterranean diet. Mediterranean diet relates to lower NAFLD prevalence because the diet is composed of more unsaturated fat instead of saturated fat. High consumption of polyunsaturated fats and the omega-3 to omega-6 balance may be associated with the low NAFLD prevalence. Although the group who follow MD did not decrease the likelihood of NAFLD, the control group has a more severe liver disease than the Mediterranean diet group [22]. What’s more, people without NASH or NAFLD are more likely to use a Mediterranean diet than patients with NASH [22, 23].

The pyramid of the Mediterranean diet is to consume plentiful wholegrain, nuts, and olive oil. Since it takes about 25 to 40% of the total calories of the daily diet, olive oil may be the most important product in the Mediterranean diet [24]. People who live in the Mediterranean region intake more olive oil instead of vegetable oil like canola oil because olive trees are native in these area and allow people to use them commonly. According to the olive oil production in 2008, at least 96.5% of olive oil was produced in the Mediterranean region [25]. Spain, Italy, and Greece are the leader of olive oil production and the top consumption of olive oil. In 2004, 36% of total olive oil production came from Spain, 27% came from Italy, and 9% from Greece. The olive oil supply per person from 1961 to 2003 in Greece was always more
than 40g in Greece and over 25g in Italy and Spain[25]. As shown in table 2, the total consumption of olive oil in the Mediterranean region is over 70% of the total consumption of olive oil [26, 27]. In other words, the total consumption of olive oil in the Mediterranean region was much greater than in the rest of the world.

Furthermore, the olive oil consumption per capita in the rest of the world is much lower than the olive oil consumption per capita in the Mediterranean area, especially in Asia. According to the olive oil consumption between 2014 to 2015, the average olive oil consumption per capita is 2.3 kg, but countries other than the Mediterranean region always lower than this average [28]. For instance, the USA is 0.9 kg per capita, Japan is 0.5 kg per capita, and Australia is 1.6 kg per capita [28]. From these olive oil consumption values, we can understand that people outside of the Mediterranean area or out of Europe will less likely consume olive oil in their daily diet. The high consumption of olive oil in daily diet might cause the low NAFLD prevalence rate in the Mediterranean area. The severity of NAFLD decreases because olive oil contains abundant monounsaturated fats that can decrease hepatic lipid accumulation in NAFLD.

Other than the high consumption of olive oil, the Mediterranean diet also contains high consumption of vegetables, fruits, and whole grains. Based on the vegetable consumption per capita from 1961 to 2017, we know that each person in the Mediterranean region always intakes over 125kg of vegetables per year. In the rest of the world, people often consume around 80kg of vegetables per year. Some countries have less than 40 kg of vegetable consumption, like the Central American countries [29]. Based on the cross-sectional study in Brazil, patients with NAFLD commonly have lower consumption of fruits, which recommended 1.5 meals with actual 0.9 meal consumption per day [30],[30]. A similar situation occurs in China. Universities staff and students with NAFLD have significantly lower consumption of fruits and vegetables than the control group [31]. Since fruits and vegetables contain a large number of micro- and macronutrients, inadequate fruit consumption might lead to a higher risk of NAFLD [30, 31]. The high consumption of fruits and vegetables in daily diet is beneficial to human health, especially lower the risk of NAFLD. Therefore, the Mediterranean diet recommends the intaking a large number of vegetables and fruits are rational.

In addition, the Mediterranean diet would consume less meat, which is considerably lower than another diet. Graph 2 and Table 3 show that the meat consumption per capita in 2013 is based on different regions. These data show that North America and Australia & New Zealand have considerably higher meat consumption, especially red meat consumption. Southern America and Europe, with the Mediterranean region, annually consume about 80kg of meat per capita. There may be some reason to cause low meat consumption in Africa and Asia. Katherine D. McManus from Harvard Medical school suggested intake of 85 to 110g portions of poultry and consuming less red meat [32]. High consumption of red meat might lead to a higher risk of NAFLD. For instance, people who intake 105g/day of red meat have significantly more NAFLD cases than people who intake 97g/day [31]. Based on table 2, Northern America and Australia with New Zealand have consumed a large amount of red meat. This excess red meat consumption might lead to the high prevalence rate of NAFLD in North America and Australia. Red meats contain large amounts of myoglobin, and meats from mammals would consider red meat, like beef and lamb. The recommended red meat consumption would be at most 200g per week, which is 10kg per capita in a year [33]. In a multivariate analysis that studies the relationship between red meat consumption and NAFLD, the high consumption of total meat, especially red or processed meat, is independently associated with NAFLD [33].

![Meat Consumption per capita (kg) 2014](image-url)

**Fig.1.** The total meat consumption (orange) and red meat consumption (blue) per capita in a different region.
According to the food consumption and NAFLD prevalence in adults of different regions (Figure 1 and Table 1) [34], the Mediterranean region consumes the largest amount of olive oil in the world. The Mediterranean region and Asia consume less meat than American and Australian countries. The Mediterranean area and Asia have higher vegetable intake than American and Australian countries. The Mediterranean area eats the largest amount of fruits in the world. Asian countries consume a relatively similar amount of fruits while comparing to western countries. The NAFLD prevalence in different regions in the world deviates somehow in terms of countries or continents. In general, the Mediterranean region has the lowest NAFLD incidence. While comparing the East and the West, they have relatively similar incidences of NAFLD [35]. While the data comparing the East and the West does not show a clear relationship between food consumption and NAFLD incidence, there is an obvious relationship between the Mediterranean diet and NAFLD incidence. Based on the food consumption between 1961 to 2013, meat, vegetables, fruits, and sweets consumption has continuously increased. The prevalence of NAFLD is parallel to the food consumption that is exponentially increasing in 10 years. With the absolute case number, China has the greatest number of cases, but the prevalence rate is lower than most countries with the highest population [36, 37]. In 2016, the U.S. had the highest prevalence rate, 26.3%, and may continuously increase to 28.4% in 2030 [36]. The countries of the Mediterranean region, like Spain, have the lowest cases number of NAFLD. However, the prediction shows that Mediterranean countries have an increasing prevalence rate in the future, and Italy may have the highest prevalence rate in 2030 [38]. The unexpected result could be caused the Mediterranean diet to become more and more unpopular among the youngest, and more than half of Italians follow a new diet that rich in red meat and butter [39]. With the diet change, the prevalence rate of NAFLD may rise exponentially in 2030.

|                | 2000   | 2001   | 2002   | 2003   | 2004   | 2005   | 2006   | 2007   |
|----------------|--------|--------|--------|--------|--------|--------|--------|--------|
| Spain          | 466.6  | 475.2  | 479.7  | 493    | 514.5  | 518.8  | 549.7  | 519.9  |
| Italy          | 744.2  | 751.1  | 775.2  | 780.4  | 805.8  | 830.1  | 828.5  | 829.3  |
| Greece         | 170.5  | 168.5  | 177.5  | 177.2  | 176.5  | 176.3  | 166.2  | 176.7  |
| Other Mediterranean | 459.586| 473.94 | 502.353| 480.6  | 503.064| 434.417| 483.678| 503.807|
| Other Europe   | 174.1  | 180.4  | 194    | 219.4  | 275.7  | 251.5  | 254.5  | 281.2  |
| Rest of World  | 368.4  | 384    | 399.6  | 387.1  | 457.2  | 468.4  | 464.1  | 522.2  |
| Total          | 2383.5 | 2436.3 | 2505.2 | 2529.2 | 2804.7 | 2650.6 | 2780.7 | 2816.7 |
Table.2. The percentage of olive oil consumption of different countries. The total olive oil consumption of that year is divided by the olive oil consumption of the specific country or area.

| Year | Spain | Italy | Greece | Other Mediterranean region | Total |
|------|-------|-------|--------|-----------------------------|-------|
| 2000 | 19.58 | 31.22 | 7.15   | 19.28                       | 77.23 |
| 2001 | 19.50 | 30.83 | 6.92   | 19.45                       | 76.70 |
| 2002 | 19.15 | 30.94 | 7.09   | 20.05                       | 77.23 |
| 2003 | 19.49 | 30.86 | 7.01   | 19.00                       | 76.36 |
| 2004 | 18.34 | 28.73 | 6.29   | 17.94                       | 71.30 |
| 2005 | 19.57 | 31.32 | 6.65   | 16.39                       | 73.93 |
| 2006 | 19.77 | 31.32 | 5.98   | 17.39                       | 72.93 |
| 2007 | 18.46 | 29.79 | 6.27   | 17.89                       | 72.06 |

Table.3. Different types of meat consumption per capita and the average meat consumption of different regions. Cite: Ritchie H, Roser M.

| Region          | Mutton and Goat | Other Meats | Poultry | Pig meat | Beef and Buffalo | Red meat | Total |
|-----------------|-----------------|-------------|---------|----------|------------------|----------|-------|
| Mediterranean Region | 2.69           | 1.91        | 21.28   | 39.54    | 15.13           | 57.36    | 80.55 |
| Europe          | 1.91           | 2.59        | 23.35   | 34.61    | 14.89           | 51.41    | 77.35 |
| Asia            | 1.94           | 0.6         | 9.79    | 15.82    | 4.4             | 22.16    | 32.55 |
| Northern America | 0.49           | 0.73        | 48.69   | 27.16    | 35.65           | 63.3     | 112.72|
| Southern America | 0.75           | 0.37        | 37      | 11.35    | 32.02           | 44.12    | 81.49 |
| Africa          | 2.78           | 1.69        | 6.73    | 1.47     | 6.33            | 10.58    | 19    |
| Australia & New Zealand | 11.34     | 2.31        | 44.32   | 23.84    | 32.02           | 67.2     | 113.83|
| World           | 1.92           | 0.98        | 14.99   | 16.02    | 9.32            | 27.26    | 43.23 |

Table.4. The summary of olive oil, meat, vegetables, and fruit consumption per capita in 2013 based on a different region in the world.

| Region          | Olive oil | Meat | Vegetables | Fruits |
|-----------------|-----------|------|------------|--------|
| Mediterranean Region | 5.89     | 80.55| 136.79     | 112.62 |
| Asia            | Not found | 32.55| 176.83     | 71.86  |
| Northern America | 2.1      | 112.72| 113.41     | 90.00  |
| Southern America | Not found | 81.49| 52.6       | 40.97  |
| Africa          | Not found | 19   | 67.57      | 66.18  |
| Australia & New Zealand | 2.06  | 113.83| 107.15     | 89.92  |
| World           | 0.42     | 43.23| 140.48     | 77.87  |
4 Policies on NAFLD

4.1 Severity of NAFLD

Nowadays, two billion people are suffering from NAFLD globally, leading to more severe diseases such as cancer and cardiovascular problems individually and healthcare and economic burden socially [1]. NAFLD is common in both western countries and Asia. The more severe form of NAFLD, NASH, is a top cause of liver cancer in western countries, whereas hepatitis B and C virus are the leading cause of liver cancer in Asian countries[2]. In Europe, NAFLD patients take up a large proportion of the European population. The disease brings a huge economic burden to the European society, indicated by the European Association for the Study of the Liver[3]. According to American Liver Foundation[4], there are approximately 100 million NAFLD patients in the US, especially among children[4]. As the number of obese population increases in Asian urban areas, NAFLD is also becoming a severe problem in Asia[4]. Considering that viral hepatitis is popular in Asia and the Asian population is more likely to have lean NAFLD, the government should make policies as soon as possible from diagnosis, control, and research perspectives [2].

4.2 Lack of Policy

Many diseases of the 21st century, such as NAFLD, are chronic diseases, but they tend to be ignored since they are not that emergent. The public health system has not taken NAFLD as an important problem, with a lack of policies and agendas[1]. For example, since the prevalence of NAFLD has only been realized recently, there is a lack of public health policy for this disease in European countries. Lazarus et al. [40] did a study to investigate the response to NAFLD in 29 European countries, and they found that nearly 100% of the countries had no strategies for this disease. There is a defect in the policy of all perspectives, including action plans, clinical treatments, and public education. There are no education programs, so most clinicians are not aware of the existence of NAFLD. A lack of primary care guideline as the core of health promotion leads to the burden of liver care. There are barely any surveillance systems from the government, resulting in a poor detection and management of NAFLD. There is also a lack of education that appeals to people to reduce sugar consumption and do more physical activities to have a healthy lifestyle to overcome obesity[40].

4.3 Lifestyle

According to data worldwide, the common, most effective way to prevent NAFLD is to prevent the risk factors such as obesity. Obesity is partly caused by the sedentary lifestyle of the modern population since the economy is developing rapidly in many western and Asian countries. Therefore, changing an unhealthy lifestyle is the key to prevent NAFLD. People should be encouraged to eat less fat and carbohydrate and do more physical activities[41].

The article written by Leoni, et al. [8] compares the guidelines of NAFLD from five associations all over the world, EASL-EASD- EASO Clinical Practice (EASL), National Institute for Health and Care Excellence (NICE), Asia-Pacific Working Party on Non-Alcoholic Fatty Liver Disease (Asia-Pacific), Italian Association for the Study of the Liver (AISF), and American Association for the Study of Liver Diseases (AASLD). Data was collected from clinicians and researchers of different disciplinary[8]. All guidelines agree that diet, physical activities, and weight loss are the center points that should be focused on to treat NAFLD. AISF guideline recommends a Mediterranean diet and low calorie intake between 1200 and 1600 kcal per day. Asia-Pacific guideline proposes that weight loss should be a gradual process. EASL, NICE, and AASLD guidelines recommend a weight loss of 7%-10% [8].

In western countries, it is acknowledged that a healthy lifestyle is currently the most effective method to treat NAFLD as there is no specific medication. Therefore, the government should encourage people to lose weight and pay attention to metabolic problems to manage NAFLD[42]. Lazarus et al. [1] also mention that reducing weight by making changes in diet and exercise and taking some promising medications help treat NAFLD.

Moreover, EASL proposes that selling fewer sugar products such as sugar-sweetened beverages in the market is necessary to reduce excess unhealthy intake. Food and drink industries should lessen their products' sugar and fat contents and label them with the exact compositions. Expert Cortez-Pinto argues that the government should make policies to restrict high-calorie food and drink advertisements on television and social media because children tend to ask for them if they see them. The government should also encourage people to do more exercise and improve their diet by publicizing healthy eating guidelines. Specifically, the Mediterranean Diet helps prevent NAFLD [3].

4.4 Diagnosis

All five guidelines of the five associations mentioned previously agree on the definition of NAFLD, which is the excessive fat in the liver and no other reason for the excessive fat. However, there is a disagreement on the definition of threshold alcohol consumption. AASLD and Asia-Pacific guidelines set a lower threshold than EASL, NICE, and AISF guidelines. As for screening, EASL, NICE, and Asia-Pacific guidelines all support screening in high-risk groups, whereas AASLD does not perceive the effect as strong enough to support screening. As for imaging, all associations agree that abdominal ultrasound (US) is the primary method of diagnosis. Asia-Pacific and EASL guidelines emphasize magnetic resonance imaging (MRI) as an important examination. Besides, the AASLD guideline treats the occurrence of many metabolic problems as a sign of NAFLD [8].

Diagnosing NAFLD and giving clinical suggestions allow patients to prevent more severe liver problems and metabolic diseases in advance. Because patients with metabolic problems such as diabetes and obesity are more likely to have NAFLD, European countries recommend systematic screening for this group of patients. On the
According to Wong and Wong’s study[2], it has been agreed in European and Asian countries that the government should support screening for people at high risk of NAFLD, mainly the patients who are more likely to have advanced fibrosis. Some formulas can make liver stiffness measurements. However, there are different standards in body mass index (BMI) between the western and Asian populations due to the disparity in the physique. To unify the definition, a conversion should be made on the fibrosis score by hospitals while deciding if a patient should do screening [2].

Although there are not many policies on NAFLD in Europe, there are suggesting policies against this disease provided by experts. Both expert Philip N. Newsome and expert Helena Cortez-Pinto propose that the government should take some actions to solve this problem. Newsome indicates that the tools that are used to diagnose NAFLD should be more advanced. Rather than using biopsy, which has limitations, the European Association for the Study of Liver Disease (EASL) is developing better diagnostic tests. Medical workers should be educated to make diagnoses as early as possible, and patients should have more knowledge about NAFLD [3].

Asian countries should also make changes to the tools. Noninvasive tools used for diagnosing NAFLD are becoming more available in Asia, so the government should allocate the equipment resource reasonably to figure out the accurate number of NAFLD patients in Asian countries. Collecting accurate data helps choose appropriate methods to manage the disease in the future[4].

Nearly all countries in the world now agree on one criterion for diagnosing MS, the risk factors of NAFLD, proposed by the American Heart Association/National Heart Lung and Blood Institute (AHA/NHLBI). The criteria include elevated waist circumference, elevated triglycerides, Low HDL-C, elevated blood pressure, and elevated fasting glucose. However, waist circumference, which can be a sign of abdominal obesity, differs from country to country due to a disparity in ethnicity and physical characteristics. For example, the criteria for Japanese are ≥ 85 cm men or ≥ 90 cm women, the criteria for Chinese are ≥ 85 cm men or ≥ 80 cm women, and the criteria for Americans and Europeans are ≥ 102 cm men or ≥ 88 cm women [41].

Another point that is worth notice is that, not similar to western countries. There are a large amount of lean NAFLD patients in Asian countries. This means that the ages of doing liver biopsy examinations for obese and lean NAFLD patients are different. Medical workers should be educated not to diagnose a non-obese patient as not having NAFLD immediately. Instead, they should consider lean NAFLD [2].

### 4.5 Treatment

All five guidelines from the five associations agree that there is currently no effective medication to treat NAFLD, so doctors should discuss the prescription with their patients. EASL guideline indicates that practitioners should only treat patients with progressive NASH pharmacologically. AASLD and Asia-Pacific guidelines propose that only patients with NASH and fibrosis can receive pharmacological treatment. The NICE guideline sets the population range to patients who have advanced liver fibrosis. AISF sets the population range to patients whose diseases are at high risk of advancement [8].

### 4.6 Research

It is important to have policies that encourage research on more effective, new drugs and more efficient ways to identify cases of NAFLD in western countries. Since there is no drug to treat NAFLD, doing examinations for the whole adult population is unreasonable. Instead, the article written by a western NAFLD study group [42] proposes that countries should focus on the population with a higher probability of having NAFLD. The epidemiology of NAFLD should be investigated further to extract this group of people. After reviewing literature data in PubMed, the NAFLD study group [42] found that factors such as age, sex, ethnicity, obesity, metabolic syndrome, and type II diabetes mellitus were critical for the development or progression of NAFLD. Having this knowledge helps make policies that make a special effort to monitor the population at a higher risk of NAFLD [42].

The research by Seto and Yuen [4] demonstrates that the NAFLD policies of Asian countries should focus on certain directions such as “lean” NAFLD and hepatitis virus. Comparing to the amount of NAFLD patients in western countries, in which the population is mostly composed of people with obesity, a large proportion of Asian NAFLD patients are suffered from “lean” NAFLD, meaning they are non-obese patients. This fact indicates that there should be solutions other than appealing to people to lose weight to prevent or treat NAFLD because one can still have “lean” NAFLD although one’s weight is reduced.

### 4.7 Organization

US supports the American Liver Foundation (ALF) as an organization dedicated to the change of public health policy related to liver diseases. ALF helps advocate liver donations, sponsors research to study liver-related diseases, and invests in liver health education. ALF spreads information to the public that liver donors are decreasing or living people whose diseases are at high risk of death and their healthy livers are transplanted into bodies of liver disease patients. ALF invests a large amount of money in research, and the organization is composed of excellent scientists and physicians. To prevent NAFLD, ALF educates people to keep a moderate weight, have a healthy diet, do exercise regularly, drink little alcohol, and be careful with taking medications in various topics through meetings. Some consultants are available every day to answer people’s questions about liver health, and social media spread information and allow people to discuss questions with others.
4.8 Social problems, patient-centered care, & coalition

Having NAFLD or not depends on not only personal behaviors but also, more importantly, public health policies. This view applies to both western and eastern countries. For example, economic inequality of the society directly causes a different diet between the wealthy and poor population because they have different access to food. The wealthy also gains more knowledge about liver health from education than the poor. They have more access to services such as physical activity facilities than the poor. Therefore, one’s socioeconomic status influences one’s NAFLD condition more than individual eating and exercising habits [1].

All over the world, policies should make sure to provide care to all NAFLD patients, including those who do not receive it now. There should be patient-centered care for NAFLD patients in a multidisciplinary way, meaning using the knowledge from many specializations. The reason is that NAFLD has some other co-morbidities, and its mechanism is closely related to body systems other than the liver, such as endocrinological and cardiovascular systems. The work of coping with NAFLD is a combination of changing the food production to transform people’s unhealthy eating habits, improving city construction to make the healthy habit more approachable, keeping a stable economy in which the gap between the rich and the poor is small, etc. Overall, NAFLD should be considered an important part of non-communicable diseases (NCDs) and global health agendas. Also, clinicians have suggested that a positive criterion instead of exclusion should diagnose NAFLD. It was suggested to rename NAFLD as MAFLD (metabolic associated fatty liver disease) to avoid acronym. Global coalitions are held to support the campaign of NAFLD. These all need efforts from researchers, medical workers, and health educators [1].

5 Conclusion

NAFLD is a multi-system disease. In addition to affecting liver health and causing liver cirrhosis and liver cancer, NAFLD also affects extra-hepatic organs and regulatory pathways and causes cardiovascular diseases. However, there are still many key issues to be solved in the pathogenesis of NAFLD, and there is no therapeutic target that can produce corresponding effective drugs at present. Therefore, the more effective treatment method for this disease is a lifestyle change.

(1) In addition to excess triglyceride and DNL, the abundance of brown adipose tissue and changes in the human microbial environment are also suspected of inducing NAFLD. Therapeutic targets related to these factors, FXR, PPAR, CCR2, and CCR5, are still in clinical transformation. However, most of the drugs designed for these therapeutic targets have significant side effects, leading to a significant reduction in the safety and efficacy of these drugs.

(2) In this case, adjustment of patients’ dietary habits and physical activities should be the first choice for NAFLD treatment. To further explore the most beneficial dietary structure for NAFLD patients, we conducted an incidence survey and dietary analysis worldwide. We found that western countries had more meat, fewer vegetables, and relatively similar fruit intake compared to eastern countries, and the NAFLD incidences of the East and the West were relatively similar. However, when we studied the Mediterranean diet recommended by EASL, there were some new findings.

(3) Comparing the global incidence of NAFLD, the prevalence of NAFLD in the Mediterranean region is significantly lower than in other regions. The high consumption of olive oil, fruits, vegetables, and whole grains and the low consumption of meat in the Mediterranean region contribute to the lower prevalence of NAFLD. This may be the reason why NAFLD has exploded around the world in recent years, as the world’s diet has shifted toward more red meat and butter.

(4) While studying the mechanism of NAFLD and good dietary habits help decrease the risk of having NAFLD, policies also play an important role. NAFLD is becoming a more serious problem in both western and eastern countries due to the increasing number of obese populations and chronic viral hepatitis. NAFLD leads to NASH and liver cancer and brings a burden to societies all over the world. Therefore, governments of both western and eastern countries must make policies from various perspectives as soon as possible. Since NAFLD is a chronic disease that is not as emergent as COVID-19, it tends to be ignored. As a result, there are few policies, agendas, and health education programs for NAFLD. Europe is an example of lacking policies for NAFLD.

(5) Since there is no medication to treat NAFLD, western countries suggest researching the epidemiology of NAFLD to monitor the population at a higher risk of the disease. Asian countries suggest doing research on MS and IR and prevent NAFLD by preventing these factors. Because “lean” NAFLD is more common in Asia than in western countries, Asian countries also need to research ways other than losing weight to prevent or treat NAFLD and the difference between obese and non-obese patients. Since hepatitis virus is an important risk factor of NAFLD in Asian countries, research on how HBV is related to NAFLD should also be done. Also, to keep people’s liver healthy, the US supports organizations such as ALF, which helps advocate liver donations, sponsors research to study liver-related diseases, including NAFLD, and invests in liver health education. Moreover, both eastern and western countries should focus on making policies that can ensure the economic equality of the society because one’s socioeconomic status influences one’s NAFLD condition profoundly. All NAFLD patients in the world should be provided with multidisciplinary patient-centered care. Works such as changing the food production, improving city construction, and keeping a stable economy all need to be accomplished. There are also global coalitions that support the campaign of NAFLD. In a word, NAFLD should be considered as an important part of the NCDs and global health agendas, and both eastern and western countries should gather power from policymakers, researchers, medical workers, and health educators to prevent or treat the disease.
(6) To put all these three concepts — mechanism, diet, and policies — together, the sources and metabolic mechanism of fatty acid in human bodies depend on food intake. Whether one gets NAFLD or not depends largely on the components of one’s diet and the amount of each of these components. Also, drugs used for treating NAFLD are developed based on fatty acid and corresponding targets. However, the drugs that have been developed currently all have problems with safety or effectiveness, so there is no specific drug for treating NAFLD, highlighting the importance of appropriate and healthy dietary habits as the most effective treatment of NAFLD now. NAFLD incidence and policies are connected by the healthy behavioral standards established by policies. In other words, good policies lead to fewer NAFLD cases. There are novel and practical policies of similar or different styles in western and eastern countries, which probably cause similar incidences of NAFLD in the East and the West. Equally importantly, the comparison and contrast between eastern and western countries teach people lessons about the prevention and treatment of NAFLD and NASH. Since the Mediterranean region has a relatively lower incidence of NAFLD than other places in the world and largely owes to the Mediterranean diet, people worldwide should consider eating less meat, more olive oil, more vegetables, and more fruits. People worldwide need to keep in mind that diet directly influences the mechanism of NAFLD, and having a healthy dietary habit is a better treatment than taking medications currently. Since all countries have different styles of policies on NAFLD and some of these policies are creative, western and eastern countries should learn from each other to figure out the best guidelines suitable for themselves to reduce NAFLD incidence. Hopefully, the comparison and contrast on NAFLD between the East and the West from the metabolic mechanism, dietary habits, and policies perspectives in this article can provide people insight into how to minimize NAFLD incidence worldwide. We are also looking forward to more future experimental or comparison studies that can reach the same goal.

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