



coffee&health

from the institute for scientific information on coffee

ROUNDTABLE REPORT

Looking after the liver:
lifestyle, coffee and caffeine

*Hosted by the Institute for Scientific Information on Coffee
in association with the British Liver Trust.*





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Overview

A roundtable of European experts from a variety of backgrounds, including academic research, medical practice and patient associations, convened at the Royal Society of Medicine, London to discuss the latest research on coffee and liver disease.

Professor Graeme Alexander, University College London and senior advisor to the British Liver Trust, and Dr Carlo La Vecchia, Professor of Medical Statistics and Epidemiology at the University of Milan, shared their knowledge and expertise with roundtable delegates, leading a discussion on the known associations between coffee intake and a reduced risk of liver disease, and the potential mechanisms behind these associations. The delegates also reflected on the importance of communicating scientific research on diet and lifestyle to liver disease patients.





Introduction

Liver disease encompasses a number of conditions including hepatitis, cirrhosis, non-alcoholic fatty liver disease, and hepatocellular cancer. A modern lifestyle, often with excess intakes of alcohol, calories and fat is associated with increased body weight, increased risk of conditions such as type 2 diabetes and heart disease, and an increase in the incidence of liver disease¹. The liver is a major organ in the body and is involved in a number of vital metabolic processes including the regulation of blood sugar and fat, the digestion of food to nutrients, and the neutralisation and detoxification of drugs and toxins. Consequently, any damage to liver cells can have a significant impact on overall health². It is likely that the links between liver disease and other conditions such as type 2 diabetes and metabolic syndrome are significant, and those who suffer with one of these conditions should be monitored for others.

A vital step in the management of liver disease is diagnosis, often made difficult as it is considered to be a 'silent' condition, or one where the disease exists initially without significant outward symptoms². Consequently, a significant proportion of sufferers are probably not aware that they have liver problems. Patient associations are striving to raise awareness of liver conditions and improve diagnosis so that those who suffer can be identified and given appropriate advice to manage their condition.

The body of research on coffee consumption and liver disease suggests that a moderate intake of coffee is associated with a reduced risk of hepatocellular cancer, cirrhosis, and fibrosis³⁻⁵. Moderate coffee consumption can be defined as 3-5 cups per day, based on the European Food Safety Authority's review of caffeine safety⁶.

"The body of research on coffee consumption and liver disease suggests that a moderate intake of coffee is associated with a reduced risk of hepatocellular cancer, cirrhosis, and fibrosis³⁻⁵."



The experts



Professor Graeme Alexander

University College London and senior advisor to the British Liver Trust, United Kingdom.



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The delegates:



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Scientific Committee ELPA/Dutch Liver Patient Association, The Netherlands.



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Steering Committee Member, Hepatitis Aid Austria — Healthy Liver Platform, Austria.



Dr JW Langer

Medical doctor, author, lecturer and medical journalist, Denmark.



Raquel Peck

CEO, World Hepatitis Alliance, United Kingdom.



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Dr David Semela

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Dr Beatrice Anfuso, PhD

Fondazione Italiana Fegato, ONLUS- Italian Liver Foundation, Italy.



Dr Trisha Macnair

Speciality Doctor/Medical Journalist, NHS, United Kingdom.



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Background

Liver disease is a significant concern across Europe, where chronic liver disease is the fifth most common cause of death⁷ and approximately 29 million people in the European Union suffer from a chronic liver condition⁸. Professor Alexander introduced the subject of liver health by highlighting the increase in Chronic Liver Disease (CLD) across Europe in recent years.



Coffee and liver disease

An extensive and growing body of research considers associations between coffee consumption and liver diseases, including hepatocellular cancer, cirrhosis, fibrosis and other liver diseases. Dr La Vecchia summarised the research, concluding that regular moderate coffee consumption is associated with a reduced risk of liver disease³⁻⁵. Moderate coffee consumption is typically defined as 3–5 cups per day, based on the European Food Safety Authority's review of caffeine safety⁶.

In reviewing the research in more detail, Dr La Vecchia discussed various aspects of liver function and associations with coffee consumption.

Chronic liver disease

is the **5th most common cause of death.**

Chronic Liver Disease is a general term for a number of conditions including:



- Non-alcohol related fatty liver disease
- Alcohol related liver disease
- Chronic hepatitis

Risk factors for Chronic Liver Disease include (but are not limited to):



Obesity



Alcohol misuse



Blood-borne viruses



Liver cancer

Liver cancer is the fifth most common cancer globally and fourteenth most common in Europe⁷. The International Agency for Research on Cancer (IARC) found no clear association between coffee intake and cancer at any body site and suggested that coffee drinking may actually help reduce the risk of certain cancers, including liver cancer⁹. Meta-analyses have suggested that coffee consumption versus no coffee consumption is associated with up to a 40% risk reduction of liver cancer, although this appears to be a dose-dependent relationship¹⁰⁻¹².

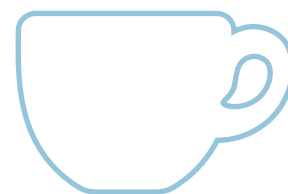
Professor Alexander suggested that it is likely that liver cancer develops from an existing liver disease, and proposed that the association between coffee consumption and a reduced risk of liver cancer may in fact link back to an effect of coffee drinking on liver disease.

Exploring the data on cancer further, Dr La Vecchia highlighted data from Finland, which suggests that the risk of liver cancer was directly related to levels of the liver enzyme GGT and inversely related to coffee drinking¹³. This research also showed a dose response effect, whereby increasing coffee intake was associated with a lower risk of liver cancer.

Cirrhosis

Research from the US¹⁴ and Italy^{15,16} suggests that coffee consumption is consistently associated with a reduced risk of cirrhosis, with a potential risk reduction of 25–70%. A greater effect was observed in patients with alcoholic liver cirrhosis.

Data has suggested that the associations between cirrhosis and coffee are consistent across different patient groups, including those with pre-existing hepatitis B and C, and those who consume alcohol¹⁶. Cirrhosis is also a condition where the incidence correlates with the incidence of liver cancer¹⁶. As mentioned by Professor Alexander, it is interesting to note that the effect of coffee consumption may be associated with a reduced incidence of diseases such as cirrhosis, conditions which may be precursors for liver cancer.



“Coffee consumption is consistently associated with a reduced risk of cirrhosis, with a potential risk reduction of 25–70%”



Chronic liver disease

Research suggests an inverse association between coffee consumption and risk of chronic liver disease, with an average risk reduction of 25–30% in low coffee consumers, and up to 65% in high coffee consumers¹⁷. A dose response relationship also appears to exist between coffee consumption and liver cancer, with a greater risk reduction observed in higher coffee consumers (50% risk reduction) compared to lower consumers (30% risk reduction)¹⁷. However, Dr La Vecchia pointed out that definitions of low and high consumers are not consistent, and tend to be study specific, dependent on levels of coffee consumed by participants. Further research is needed to help define the amount of coffee consumption in relation to chronic liver disease risk reduction.

A central role for liver enzymes?

The liver is a complex organ that plays a pivotal role in many metabolic processes within the body. Damage or inflammation of the liver can manifest as raised levels of liver enzymes, and a number of researchers have specifically investigated levels of liver enzymes in relation to coffee consumption⁵.

Coffee consumption has been inversely associated with the activity of the liver enzyme gamma-glutamyl transferase (GGT) in studies from Japan, Europe and the USA^{18,19}. Data from different countries is particularly valuable as it suggests an effect in genetically different populations. Data from Japan suggests that GGT levels were approximately 30% lower in those who drank 5 or more cups of coffee per day, compared to non-drinkers¹⁸. Those who regularly consume alcohol tend to have higher GGT levels initially, and the coffee consumption seems to have a greater effect in these individuals¹⁹.

Further research also suggests that coffee consumption is associated with an approximate 40% reduction in risk of elevated levels of the liver enzyme ALT²⁰.





Coffee components and potential mechanisms

Dr La Vecchia considered the potential mechanisms that may explain the association between coffee consumption and reduced risk of liver disease. Although the precise mechanisms remain unclear, he suggested that the number of components found in coffee could explain the effect, including caffeine, coffee oils, kahweol and cafestol and antioxidants. Although current data does not enable firm conclusions to be drawn, the data suggesting that a moderate intake of coffee is associated with a reduced risk of a variety of liver conditions was particularly interesting to the roundtable members³⁻⁵.

Delegates commented that there is a vast range of coffee beverages available today and questioned whether the different preparation methods have different impacts on liver function. Unfortunately, the limited information available does not enable conclusions to be reached. One large study from Finland reported that coffee intake was inversely associated with liver cancer, irrespective of whether the coffee was boiled or filtered²¹. Authors of a further review of associations between coffee intake and liver fibrosis suggested that conventional filtered coffee is the form generally used in most published studies, supporting its protective role²².

Some possible negative effects of coffee consumption include anxiety or jitteriness (i.e. feeling on edge or uneasy) but most individuals tend to self-limit their caffeine consumption if they are thus affected.

Metabolic syndrome, liver health and coffee — are they associated?

Dr La Vecchia introduced the suggestion that 'metabolic syndrome', a combination of obesity, hypertension and type 2 diabetes, is associated with liver function and sufferers have a greater risk of liver cancer, initiating a discussion about potential associations between metabolic syndrome, insulin resistance, liver health and coffee consumption.

Research suggests that a moderate intake of coffee is associated with a reduced risk of type 2 diabetes^{23,24} in addition to reduced risk of liver diseases. Dr La Vecchia suggested that a potential link between coffee consumption may be associated with a reduction in insulin resistance, which in turn may improve outcomes for diabetes and liver health²⁵.

Other roundtable members expressed an interest in such associations, suggesting that metabolic syndrome may be worse in those with fatty liver disease. Professor Alexander has a particular interest in senescence (or ageing) of the liver, and suggested that there is an association between this and diabetes.



Diagnosis — the tip of the iceberg?

One of the main issues discussed at the roundtable was the diagnosis of liver disease, and the fact that a majority of sufferers are unaware of their condition.

Even though the liver is a vital organ, the perception in some European countries is that liver health is not considered as high a priority as other conditions, such as heart disease. For example, while, an attendee from the British Liver Trust suggested that the public actually does consider liver disease to be very serious, this is not the case in Germany.

A patient's history is critical to support a diagnosis of liver disease, particularly levels of alcohol intake, blood pressure, risk of type 2 diabetes and Body Mass Index (BMI), although some roundtable members questioned the use of BMI as an appropriate measure, suggesting waist circumference may be a better indicator of body fatness. A variety of other tests are available including blood tests for liver function and fibrosis, and liver scanning.



“Even though the liver is a vital organ, the perception in some European countries is that liver health is not considered as high a priority as other conditions, such as heart disease.”

Improving communication beyond the consulting room

Roundtable members from various European patient associations, including transplant groups and liver health patient organisations, discussed the importance of communication to patients about healthy lifestyles, including information about coffee consumption.

They highlighted the fact that patient associations can play a specific role in providing information and education on health aspects of diet specific to their condition, often acting as a link between the medical profession and the patients. Bridging the gap can help patients access information in a manner that is straightforward and easy to understand, indeed the medical



“A moderate intake of coffee of 3–5 cups a day is associated with a beneficial effect on liver health^{3,4}”



professionals at the roundtable suggested that patient to patient advice is often rated highly and potentially more likely to be acted upon than advice from a health professional.

The roundtable members felt that understanding risk factors associated with the progression of liver diseases could be a motivating factor. For example, if a patient was aware they had hepatitis they would be more likely to address diet and lifestyle factors that could help them manage their condition.

A moderate intake of coffee of 3–5 cups a day is associated with a beneficial effect on liver health^{3,4}, a fact that struck a chord with many of the delegates who work in patient associations. Patients often have a negative opinion of coffee and are not given proactive advice on coffee consumption as part of a healthy lifestyle. However, roundtable delegates felt that patients could benefit from such advice.





In summary

An increasing incidence of liver disease across Europe, associated in some cases with increases in metabolic syndrome, type 2 diabetes and obesity, is concerning, despite the fact that it is likely that diagnosed cases of liver disease represent only a small proportion of those with the condition. Physicians and patient associations are striving to improve diagnosis and subsequent treatment of liver conditions, as well as providing meaningful preventative advice to stem the increasing incidence. Research consistently suggests that moderate coffee drinking (defined as 3–5 cups per day by EFSA) is associated with a reduced risk of liver disease^{3,4}.

About ISIC

The Institute for Scientific Information on Coffee (ISIC) is a not-for-profit organization, established in 1990 and devoted to the study and disclosure of science related to “coffee and health.” Since 2003 ISIC also supports a pan-European education programme, working in partnership with national coffee associations in nine countries to convey current scientific knowledge on “coffee and health” to health care professionals.

ISIC’s activities are focused on:

- the study of scientific matters related to “coffee and health”
- the collection and evaluation of studies and scientific information about “coffee and health”
- the support of independent scientific research on “coffee and health”
- active dissemination of balanced “coffee and health” scientific research to a broad range of stakeholders.

ISIC respects scientific research ethics in all its activities. ISIC’s communications are based on sound science and rely on scientific studies derived from peer-reviewed scientific journals and other publications.

ISIC members are six of the major European coffee companies: illycaffè, Jacobs Douwe Egberts, Lavazza, Nestlé, Paulig, and Tchibo.

About coffeeandhealth.org

The website www.coffeeandhealth.org is a science-based resource developed for health care and other professional audiences and provides the latest information and research into coffee, caffeine and health.

Follow us on twitter: @coffeeandhealth

About the British Liver Trust

The British Liver Trust is the largest UK charity for all adults with liver disease. It tackles the serious and growing public health problem of liver disease. Liver disease is the third leading cause of premature death and more than one in five of us are at risk of developing the condition. The British Liver Trust provides up to date information and support and campaigns for improved services and care. Its Love Your Liver campaign encourages the best possible liver health for all through encouraging prevention, raising awareness of the risk factors and promoting early detection.



www.britishlivertrust.org.uk



References

1. WHO (2014) 'Global Status Report on Noncommunicable Diseases'. World Health Organisation, Geneva. Available at: <http://www.who.int/nmh/publications/ncd-status-report-2014/en/>
2. British Liver Trust 'Liver Health'. Available at: <https://www.britishlivertrust.org.uk/liver-information/>
3. Saab S. et al. (2014) Impact of coffee on liver disease a systematic review. *Liver Int*, 34(4):495–504.
4. Wadhawan M. and Anandt A.C. (2016) Coffee and Liver Disease. *J Clin Exp Hepatol*, 6(1):40–46.
5. Heath R. et al. (2017) Coffee: The magical bean for liver diseases. *World J Hepatol*, 9(15):689–698.
6. EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA) (2015) Scientific Opinion on the safety of caffeine. *EFSA Journal*, 13(5):4102.
7. European Association for the Study of the Liver (2013) 'The burden of Liver Disease in Europe: A Review of Available Epidemiological Data'. Available at: http://www.easl.eu/medias/EASLimg/Discover/EU/54ae845caec619f_file.pdf
8. Eurostat (2007) 'Europe in Figures: Eurostat yearbook 2006-07'. Available at: http://www.nefmi.gov.hu/letolt/eu/ks_cd_06_001_en.pdf
9. Loomis D. et al. (2016) Carcinogenicity of drinking coffee, mate, and very hot beverages. *Lancet Oncol*, 17(7):877–878.
10. Bravi F. et al. (2007) Coffee drinking and hepatocellular carcinoma risk: a meta-analysis. *Hepatol*, 46:430–435.
11. Larsson S.C. et al. (2007) Coffee consumption and liver cancer: a meta-analysis. *Gastroenterol*, 132:1740–1745.
12. Bravi F. et al. (2013) Coffee reduces risk for hepatocellular carcinoma: An updated meta-analysis. *Clin Gastro and Hepatol*, 11:1413–1421.
13. Hu G. et al. (2008) Joint effects of coffee consumption and serum gamma-glutamyltransferase on the risk of liver cancer. *Hepatol*, 48(1):129–36.
14. Klatsky A.L. et al. (1993) Coffee, tea, and mortality. *Ann Epidemiol*, 3(4):375–81.
15. Corrao G. et al. (1994) The effect of drinking coffee and smoking cigarettes on the risk of cirrhosis associated with alcohol consumption - A case-control study. *Europ J Epidemiol*, 10 (6):657–664.
16. Gallus S. et al. (2002) Does coffee protect against liver cirrhosis? *Ann Epidemiol*, 12(3):202–5.
17. Bravi F. et al. (2016) Coffee and the risk of hepatocellular carcinoma and chronic liver disease: a systematic review and meta-analysis of prospective studies. *Eur J Cancer Prev*, 26(5):368–377.
18. Kono S. et al. (1994) Coffee and serum gamma-glutamyltransferase: a study of self-defense officials in Japan. *Am J Epidemiol*, 139(7):723–7.
19. Tanaka K. et al. (1998) Coffee consumption and decreased serum gamma-glutamyltransferase and aminotransferase activities among male alcohol drinkers. *Int J Epidemiol*, 27(3):438–43.
20. Ruhl C.E. and Everhart J.E. (2005) Coffee and caffeine consumption reduce the risk of elevated serum alanine aminotransferase activity in the United States. *Gastroenterol*, 128(1):24–32.
21. Lai G.Y. (2013) The association of coffee intake with liver cancer incidence and chronic liver disease mortality in male smokers. *Br J Canc*, 109:1344–1351.
22. Dranoff J.A. (2017) How does coffee prevent liver fibrosis? Biological plausibility for recent epidemiological observations. *Hepatol*, 60(2):464–467.
23. Jiang X. et al. (2014) Coffee and caffeine intake and incidence of type 2 diabetes mellitus: a meta-analysis of prospective studies. *EJCN*, 53(1):25–38.
24. Ding M. et al. (2014) Caffeinated and decaffeinated coffee consumption and risk of type 2 diabetes: A systematic review and dose response meta-analysis. *Diab Care*, 37(2):569–586.
25. Van Dam R.M. et al. (2002) Coffee consumption and risk of type 2 diabetes mellitus. *Lancet*, 360:1477–1478.