Complementary
Medicine Research

Complement Med Res , DOI: 10.1159/000540668
Received: April 3, 2024
Accepted: July 30, 2024
Published online: August 9, 2024

Fasting in Science and Clinics - A Report on Proceedings from the International Scientific Symposium and Conference on Fasting in Berlin (June 2023)

Breinlinger C, Meiß S, Hanslian E, Jordan S, Boschmann M, Rajput Khokhar A, Michalsen A, Koppold DA

ISSN: 2504-2092 (Print), eISSN: 2504-2106 (Online)
https://www.karger.com/CMR
Complementary Medicine Research

Fasting in Science and Clinics - A Report on Proceedings from the International Scientific Symposium and Conference on Fasting in Berlin (June 2023)

Fasten in Wissenschaft und Klinik - Ein Bericht über die Ergebnisse des internationalen wissenschaftlichen Symposiums und Konferenz in Berlin zum Thema Fasten (Juni 2023)

Carolin Breinlinger[a], Sara Meiß[b,c], Etienne Hanslian[b,c], Stefan Jordan[d], Michael Boschmann[e], Anika Rajput Khokhar[b,f], Andreas Michalsen[a,b], Daniela A. Koppold[a,b,g]

[a] Charité Competence Center for Traditional and Integrative Medicine (CCCTIM), Charité – Universitätsmedizin Berlin, Corporate Member of Freie Universität Berlin, Humboldt-Universität zu Berlin and Berlin Institute of Health, Berlin, Germany

[b] Institute of Social Medicine, Epidemiology and Health Economics, Charité – Universitätsmedizin Berlin Corporate Member of Freie Universität Berlin and Humboldt-Universität zu Berlin, 10117 Berlin, Germany.

[c] Department of Internal Medicine and Nature-Based Therapies, Immanuel Hospital Berlin, 14109 Berlin, Germany.

[d] Department of Microbiology, Infectious Diseases and Immunology, Charité – Universitätsmedizin Berlin, Berlin, Germany.

[e] Experimental and Clinical Research Unit, Joint collaboration between Max-Delbrück-Center and Charité – Universitätsmedizin Berlin, Berlin, Germany.

[f] Department of Dermatology, Venereology and Allergology, Charité – Universitätsmedizin Berlin, Corporate Member ofFreie Universität Berlin and Humboldt-Universität zu Berlin, Berlin, Germany.

[g] Department of Pediatrics, Division of Oncology and Hematology, Charité – Universitätsmedizin Berlin, Corporate Member of Freie Universität Berlin and Humboldt-Universität zu Berlin, 10117 Berlin, Germany.

Corresponding Author: Carolin Breinlinger, +49 30 80505-614
E-mail address: carolin.breinlinger@charite.de

Short title: Fasting in Science and Clinics - A Conference Report

Kurztitel: Fasten in Wissenschaft und Klinik - Ein Tagungsbericht

Abstract

Background: A fasting conference and scientific symposium on fasting were held in Berlin in June 2023. Researchers and clinicians from around the world shared new findings, clinical insights, and work in progress during a three-day program.
Summary: Different fasting regimens, including prolonged, short-term, intermittent fasting and time-restricted eating (TRE) were discussed for preventive and therapeutic settings. Experimental and clinical findings shared ranged from biochemical and cellular fasting responses to fasting-mimicking agents, the role of the gut microbiome and immunological effects. Clinically, a special focus was placed upon metabolic, autoimmune, neurodegenerative, and oncological diseases. The discussion also covered how modern technologies, practical adaptations to traditional protocols, and a supportive network of specialized physicians can assist in the practical application of fasting, among other subjects.
Key Messages: Dose-response relationships, gender aspects, and the subjective experience of fasting seem promising for future research, while further investigation of religious fasting may offer deeper insights into motivational and health aspects.

Keywords

Fasting, Intermittent Fasting, Prolonged Fasting, Nutrition, Conference

Zusammenfassung

Hintergrund: Im Juni 2023 fanden in Berlin eine Fastenkonferenz und ein wissenschaftliches Symposium zum Thema Fasten statt. Forscher:innen und Kliniker:innen aus der ganzen Welt tauschten in einem dreitägigen Programm neue Erkenntnisse, klinische Einsichten und laufende Arbeiten aus.
Zusammenfassung: Es wurden verschiedene Fastenformen, darunter angzeitfasten, Kurzzeitfasten, intermittierendes Fasten und zeitlich begrenztes Essen (TRE), für präventive und therapeutische Zwecke diskutiert. Die vorgestellten experimentellen und klinischen Ergebnisse reichten von biochemischen und zellulären Fastenreaktionen bis hin zu Fasten nachahmenden Substanzen, der Rolle des Darmmikrobioms und immunologischen Auswirkungen. In klinischer Hinsicht wurde ein besonderer Schwerpunkt auf Stoffwechsel-, Autoimmun-, neurodegenerative und onkologische Erkrankungen gelegt. In der Diskussion wurde auch erörtert, wie moderne Technologien, praktische Anpassungen traditioneller Protokolle und ein unterstützendes Netzwerk spezialisierter Ärzt:innen bei der praktischen Anwendung des Fastens helfen können.
Schlussfolgerung: Dosis-Wirkungs-Beziehungen, geschlechtsspezifische Aspekte und das subjektive Erleben des Fastens scheinen vielversprechend für künftige Forschungen, während weitere Untersuchungen zum religiösen Fasten tiefere Einblicke in motivationale und gesundheitliche Aspekte bieten könnten.
Schlüsselwörter
Fasten, Intermittierendes Fasten, Langzeitfasten, Ernährung, Konferenz

1 Introduction

As literature on fasting is growing, public awareness is increasing, and potential clinical applications are multiplying. Whether in oncology or for obesity and type 2 diabetes mellitus, in neurodegenerative diseases or for preventive purposes: fasting seems to fit them all [1-3]. Basic research has described the biochemical pathways and physiological regulatory mechanisms promoting this vast array of positive health effects. And yet there is still much to explore. Namely, different processes related to autophagy, fasting-mimicking molecules or microbiome changes mediated by fasting are currently being studied by different research groups around the world. In the meantime, translation into clinical practice is challenging. Dose-response patterns seem to differ not only between individuals but also within the individual, depending on activity, diet and chronobiological patterns. Intermittent fasting, short-term and long-term fasting are applied to a variety of diagnoses, but they have so far not been compared to each other concerning efficacy, compliance, or adverse effects. The field of oncology poses its own challenges, with a variety of diagnoses and novel therapies requiring adaptive fasting schemes. Regarding metabolic diseases, long-term behavioral and motivational aspects are among the points to consider. At the same time, aspects of religiosity and/or spirituality matter to a vast majority of people who fast every year worldwide, but these are rarely considered in medical contexts.

Taken together, there is a multitude of unresolved questions –and the diversity of experimental, translational, and clinical researchers worldwide dedicated to their exploration is impressive. For this reason, a research group at Charité – Universitätsmedizin Berlin, in cooperation with the Medical Association for Fasting and Nutrition (ÄGHE) and the Immanuel Hospital Berlin hosted the 20th International Fasting Conference on the 24th-25th of June 2023, preceded by a scientific symposium on the 23rd of June.

At the conference, speakers from Germany, Austria, Luxembourg, Italy, and the USA addressed an audience of a total of 200 participants on site and an additional 130 participants online. International guests from over 10 countries and 3 continents attended. The conference focused on the medical use of fasting in prevention and therapy.

The preceding scientific symposium was attended by 60 scientists from around the globe. In addition to discussing the current state of fasting research and research gaps, this symposium also aimed to address open questions that may lead to new collaborations and to promote young scientists. Two workshops focused on translational topics, while work in progress was presented in 15 short lectures and 13 posters.

The following overview presents the topics covered and summarizes the most prominent points addressed during the presentations at the symposium and conference.

2 Topics

2.1 Experimental and Translational Aspects of Fasting

2.1.1 Translational Metabolism Research

Fasting is associated with complex changes in both systemic and local, organ-specific energy metabolism. However, these changes are still not comprehensively analyzed. Dr. Boschmann (Clinical Research Unit at the Experimental & Clinical Research Center, Max Delbrück Center / Charité Universitätsmedizin Berlin (ECRC)) presented suitable methods, such as non-invasive indirect calorimetry or the minimally invasive microdialysis that should be more frequently used to ascertain systemic, local, and tissue-specific effects for different forms of fasting.

Mr. Bajaj (University of Bonn) pointed out the complexity of the fasting metabolism at the molecular level, demonstrating the profound influence of the fasting state on the proteome, serum lipidome, and fatty acid oxidation mechanisms in human peripheral blood mononuclear cells. As a result, integrating multi-omic (analytical approach including data such as the genome, proteome, transcriptome, epigenome, metabolome, and/or microbiome) level analyses could offer broad therapeutic potential centered around proteostatic systems, such as autophagy, intimately linked to mitochondrial fatty acid oxidation. A fasting state also influences the proteome and fatty acid oxidation mechanisms. As a result, intestinal stem cell function, hormonal metabolic pathways and epigenetics are affected, offering a broad therapeutic potential [4].

Biochemist and molecular biologist Prof. Eisenberg (University of Graz) presented updates from research around fasting mimetics, such as the natural polyamine spermidine and the B3 vitamin nicotinamide. These natural substances can imitate certain effects of fasting, such as increasing autophagy or autophagy competence of cells, leading to an increase in lifespan. In animal models, researchers have discovered that fasting mimetics exert broad cardiovascular and neuroprotective effects [5-7]. Ms.Krivogradand Y. Liang (FU Berlin) outlined that spermidine not only protected fruit flies from mitochondrial dysfunction and cognitive decline, but also slowed down locomotive decline[8].Preliminary results from epidemiological cohort studies in humans indicate a risk reduction of age-associated diseases by a spermidine-rich diet [5, 9]. First intervention studies are presently being conducted with spermidine-rich wheat germ extracts, which are investigated as dietary supplements [10].

2.1.2 E-Health

Ms. Manlik (Hasso Plattner Institute (HPI), University of Potsdam) presented different machine learning models that used continuous glucose monitoring data and acceleration data of fasting states. This tool allowed the tracking of dietary adherence in patients that practiced time-restricted eating (TRE). Although the models need further improvement, they could be used as tools for assessing compliance in future fasting studies [11]. Prof. Bert Arnrich (HPI) underpinned the necessity of sensor data for nutritional medicine and fasting, as they are increasingly able to measure metabolic data in real time, track other relevant behavioral changes and simultaneously provide personalized recommendations [11].

2.1.3 Gut Microbiome Research

Mr. Maifeld (ECRC) presented data from a multicenter randomized controlled study of 71 hypertensive patients with metabolic syndrome. The intervention group (n=35) underwent a 5-day Buchinger therapeutic fasting followed by a 3-month modified Dietary Approach to Stop Hypertension (DASH) diet. The control group (n=36) only followed the modified DASH diet for 3 months. The intervention not only resulted in a significant long-term reduction in body weight and improvement in systolic blood pressure levels. It also yielded changes in the gut microbiome that translated into increased production of short-chain fatty acids, which was not observed in the control group (clinicaltrials.gov, NCT02099968).

2.2 Fasting for Human Health

In clinical research, it is not uncommon to find publications on fasting that use similar terminology but mean different regimens. Ms. Breinlinger (Charité – Universitätsmedizin Berlin) presented the methodology, results and challenges of an international consensus process on fasting terminology involving 38 experts from around the world. Twenty-four definitions emerged from this process. This terminology is to be published soon and is hoped to facilitate future research and science communication (clinicaltrials.gov, NCT05668156).

Patients often ask whether fasting can be combined with sports. Prof. Zopf (Universitätsklinikum Erlangen) presented studies on alternate-day fasting and TRE from the field of competitive sports [12]. Longer fasting intervals involving sports have not been studied yet, although moderate exercise is a constituent element of prolonged fasting protocols. Studies on intermittent fasting in competitive sports in women and men indicate that fat mass decreases, while the fat-free body mass is maintained, and performance remains the same. One study demonstrated that TRE did not affect running performance in male endurance runners [13]. Performance tests in another investigation showed no significant differences between TRE and ad libitum eating while the peak power

output to body weight ratio improved in the TRE group. This could be attributed to the weight loss observed [14]. People with obesity who practiced intermittent fasting and light exercise at the same time showed an increase in muscle mass, in contrast to people who only fasted [15]. As increased muscle mass is known to possess anti-inflammatory and immune-stabilizing effects. Prof. Zopf recommends exercise in combination with intermittent fasting for both high-performance athletes and people who are overweight. Regarding the combination of intermittent fasting and physical activity in cancer patients, recommendations should depend on the type of cancer and the type of cancer treatment.
Dr. Mähler (ECRC) presented results of a randomized, waitlist-controlled study on the physiological effects of a 5-day Buchinger fasting regimen in 38 healthy men and women (clinicaltrials.gov, NCT04452916). Cardiometabolic effects during fasting were decreases in mean resting energy expenditure (70 kcal/d), body weight (4.4 kg), body fat (2.0 kg), systolic (3.1 mmHg) and diastolic blood pressure (4.5 mmHg). Twelve weeks after fasting, energy expenditure and blood pressure returned to baseline values whereas the body fat loss of 2 kg remained stable.

Ms. Nicoubin (German Federal Agency for Civic Education) gave an insight to fasting from a different perspective. As fasting traditions have a firm place in almost all religious traditions [16]. It seems worthwhile for research to tap into motivational and behavioral aspects of this. From the perspective of the Baha'i religion, which Ms. Nicoubin focused on, fasting is not seen as hostile to the body, but as a primarily spiritual practice. Bahá’ís worldwide follow an intermittent dry fast for 19 days every March. The physical aspect of refraining from food and drink for a short period of time can be seen as a symbol of spiritual restraint from worldly attachments. Among other aspects this can promote discipline, as well as physical and mental health [17]. The different aspects involved in religious fasting make it a health-related behavior of interest from clinical, psychological, and public health perspectives.
2.3 Fasting in Prevention and Therapy
2.3.1 Applications in Metabolic Diseases
Intuitively, metabolic disorders are of the main targets of fasting interventions. Prof. Schwarz reported on his experience with 2-week water fasting in the diabetological department of the University Hospital of Dresden (Universitätsklinikum Dresden Carl Gustav Carus). According to his experience, this dietary intervention produces a significant decrease in the fatty liver index, which he was unable to achieve with other pharmacological or lifestyle interventions. So far, he has not noted any relevant side effects in over 400 patients. Preliminary data presented by Mr. Rüther (Charité—Universitätsmedizin Berlin) showed that the application of a hypocaloric formula diet (600-800 kcal/d) followed for 3 months induces relevant diabetes remission rates (clinicaltrials.gov, NCT05295160). The success of the intervention seemed to depend on the time since diagnosis rather than on BMI. Regarding obesity most studies to date have concentrated on intermittent fasting regimens. Recent data from the USA with 90 obese subjects have shown that a time-restricted 16:8 diet (eating from noon to 8 pm, without calorie counting) has a similar effect on weight loss (5% of total weight) after one year as a diet with a constant 25% calorie restriction (CR, i.e. normal diet - 500 kcal) [18]. Prof. Varady (University of Illinois, Chicago) emphasized the importance of exercising to limit muscle mass loss while practicing TRE or CR for weight loss. Her team was able to show that TRE often naturally leads to a reduction in daily energy intake of about 400 kcal per day, just through the restriction of meals to a specific eating window [18]. For this reason, TRE may be easier to incorporate into daily life than caloric restriction, which requires consistent calorie counting. In addition, TRE has been shown to improve insulin sensitivity and to be effective for weight maintenance. In their studies, Prof. Varady and her team also found that the early TRE window (eating between 8 a.m. and 4 p.m.) was better for blood glucose control, but that the late TRE window (eating between 12 p.m. and 8 p.m.) was usually better adhered to. Generally, it seems important for the effects of TRE to maintain a consistent eating window (+/- 1 hour) [18, 19].
Comparing the effects of 6 months 16:8 TRE to daily calorie restriction and a control diet on body weight and glycemic control in adults with type 2 diabetes mellitus, Ms. Pavlou (University of Illinois, Chicago) reported that significant weight and body fat loss was achieved in the TRE group compared to the control group. However, compared to the CR group, the weight loss in the TRE group was not significantly greater. HDL-levels and other cardiometabolic risk factors as well as glycemic control were not influenced by either intervention. Similarly, a study presented by Ms. Lin (University of Illinois, Chicago) on adults with obesity practicing 16:8 TRE for 12 months did not show additional cardiometabolic benefits to a 25% daily caloric restriction. Nonetheless, both diets significantly improved weight and insulin sensitivity when compared toa control diet [18].

Studying the chronobiological components of TRE, Dr. Ramich (German Institute of Human Nutrition, DIfE) presented preliminary data on the ChronoFast cross-over study [20], which examined the effects of a 2-week early TRE (8:00 a.m. to 4:00 p.m.) versus late TRE (1:00 p.m. 9:00 p.m.), isocaloric to the usual diet, on cardiometabolic health, inflammation, and sleep in 31 women with obesity and increased risk of type 2 diabetes mellitus. The different time windows for food intake affected the circadian patterns of the organism and insulin secretion, while all other parameters showed no intergroup differences.

2.3.2 Applications in Oncology

One of the novel emerging fields of fasting research during the last decade has been its applications in oncology. Dr. Vernieri (Istituto Nazionale dei Tumori & Italian Association for Cancer Research) shared study results on fasting mimicking diets (FMD) that have shown a variety of antitumor effects in vitro as well as in preclinical models and clinical application. Among others, they reduce blood insulin and blood glucose concentration [21] and can reduce immunosuppressive cell subsets, while boosting systemic and intratumor immunity [22]. These effects were found independent of tumor type, concomitant treatment and disease stage in the studies performed until now at the National Tumor Institute of Italy.

Since oncology is a very innovative field, new therapies and their possible combination with fasting interventions raise questions that need to be continually explored. Dr. David (Tel Aviv Sheba Medical Center) shared thoughts on potential synergies of Immune Check Point Inhibitors (ICIs) with FMD. She presented a recent study about fecal microbiota transplant affecting the response rates and reducing side effects of ICIs in previously non-responder advanced melanoma patients. As fasting is known to affect the gut microbiota rapidly, she presented the hypothesis that FMD in combination with immunotherapy could strengthen the immune system activity through microbiome manipulation resulting in improved treatment outcomes and reduced adverse events. At the moment, her team is exploring whether the gut microbiome could be a possible mediator for synergies between FMDs and ICIs [23, 24].

A team from the University Clinic of Mainz on the other hand is exploring how intermittent fasting could potentially support chemotherapy in gynecological patients. Dr. Schmidt (University Medical Center of Johannes Gutenberg University of Mainz) shared the protocol of an RCT on TRE (16:8)during chemotherapy, where data on fatigue and general quality of life are presently beingcollected [25].

Prof. Michalsen's team has been researching short-term fasting as an adjunct to standard chemotherapy in breast cancer patients for nearly a decade. The results of their recent multicenter RCT are currently being evaluated, but some practical insights were shared: In their experience, breast cancer patients show a high motivation for dietary interventions including short-term fasting. The close accompaniment by a nutritionist was well received. Short-term fasting for 60 to 72 hours with a daily intake of <200 kcal was feasible during chemotherapy. Caloric intake consisted of vegetable juices and broths. Insulin peaks through fruit juices should be avoided. A few patients complained that the taste of celery was very unpleasant during chemotherapy, so patients were advised to avoid it. If after cortisone medication hunger was a problem, oat broth or one to two potatoes boiled in their skin usually helped to overcome the complains. The oat broth also helped with nausea, while a low dose of magnesium sulfate was given in obstipated patients (clinicaltrials.gov, NCT03162289).

2.3.3 Effects of Fasting on the Immune System, Autoimmune Diseases, and Chronic Inflammation

Another topic addressed during the conference was that of chronic inflammation. Dr. Jordan introduced the topic, demonstrating his findings on pro-inflammatory monocytes [26]. These seem to migrate from the blood into the bone marrow during fasting, with this process being reversed during refeeding. Along this line, Prof. Hoffmann (University Hospital Schleswig-Holstein and Universität zu Lübeck) shared preliminary results on alternate-day fasting in mice largely preventing the perpetuation of inflammation in an arthritis model.

Challenges for further studies lie in identifying the links between disease-relevant systemic and cellular metabolic changes. This is one of the objectives of the ExpoBiome study, a multicenter clinical trial financed by the European Union, investigating the association of the gut microbiome-derived molecular complex (including nucleic acids, polypeptides, and metabolites) and inflammatory diseases through the examples of Parkinson's disease (PD) and rheumatoid arthritis (RA). The specific aims of the study presented by Ms. Hansen (Luxembourg Centre for Systems Biomedicine) include identifying microbial taxa and molecules related to chronic diseases, validating biomarkers during microbiome-targeted interventions like therapeutic fasting, and pinpointing novel anti-inflammatory therapy targets through personalized gut-on-chip models [27]. As part of the study,30 participants with PD and RA respectively were subjected to a week of prolonged fasting followed by TRE for a period of 12 months, with nutritional, microbial and immunological data being collected and analyzed. Preliminary findings indicate significant improvements in RA symptoms after prolonged fasting, but these changes are less

pronounced in PD patients, leading to the suggestion that further exploration may clarify the distinct impacts of fasting on the immune system and the potential function of the gut microbiome in mediating some of these effects.

That certain dietary regimens are correlated with improved cognitive functions in neurodegenerative diseases was shown by Ms. Hebah (University of Luxembourg), who presented the results of a meta-analysis of 25 controlled epidemiological trials including the Mediterranean, Western, ketogenic, time and caloric restriction diets. Also Dr. Bahr (ECRC) presented preliminary data on the effects of fasting versus ketogenic diet versus controls on Multiple Sclerosis patients, showing a stabilization of disease activity, improved metabolic and partly neuropsychiatric outcomes. Likewise, the FASTA study (Ms. Meiß/Ms. Alvarado-Rupflin (Immanuel Hospital Berlin & Charité – Universitätsmedizin Berlin) examining patients suffering from osteoarthritis, fibromyalgia, or RA and being treated with a multimodal approach including prolonged fasting showed favorable results on the disease-specific functional and psychological well-being for all diagnoses [28]. Whether these effects could be utilized in supporting Long COVID patients through prolonged fasting is currently being studied by Ms. Gomez-Bravo et al. (Centre Hospitalier Neuro-Psychiatrique, Ettelbrück, Luxembourg).

Thus, it was no surprise when Dr. Pappe (Charité—Universitätsmedizin Berlin), the first dentist to ever speak at a fasting congress, presented data on the relationship between systemic and oral inflammation. She shared data from different studies indicating that fasting interventions, whether prolonged or intermittent, were observed to decrease inflammation in periodontitis.

2.4 Specific Therapeutic Regimens

One of the specific therapeutic fasting regimens presented at the conference was dry fasting. Dr. Papagiannoupoulou (Medical Practitioner in Athens, Greece) presented results from her research on the physiological effects of a 5-day dry fast (DF), inducing three stressors: Hypovolemia, Hypertonicity, and Hypoglycemia. DF led to a decrease in adrenaline and erythropoietin, which suggests an improvement in cell oxygen supply [29]. Additionally, improved kidney function was demonstrated through an increase in the Glomerular Filtration Rate [30], a result of the increase in Vasopressin [29]. An upregulated HPA-axis also indicates a strong immune-stimulating effect of DF [29]. Furthermore, she discussed not-yet-published results concerning changes in hormones affecting the blood-peripheral cell interphase, blood glucose regulation, and anti-atherosclerotic effects, revealing potential applications and benefits of this fasting regimen (Papagiannopoulou MI, Papagiannopoulos-Vatopaidinos IE, Dotsika EN, Sideris VI. Dry Fasting Physiology: Responses to Hypoglycemia (to be published)).

A more widely known fasting regimen was presented by Dr. Mesnage, sharing insights from recent studies on long-term fluid-only fasting at the Buchinger-Wilhelmi Clinics. Effects included a decrease in waist circumference and LDL cholesterol, weight loss, and a reduction in blood pressure in patients with grade 2 hypertension. Muscle strength, on the other hand, increased, and preliminary data also show oral microbiome changes and a decrease in inflammatory markers in gingival fluid [1, 31].

Studies on the use of FMDs and their clinical application are also ongoing. Ms. May (Charité—Universitätsmedizin Berlin) presented the methodology of a study on subfertility, using a 5-day FMD three times over 6 months to improve sperm quality. In addition to the quantitative analyses planned, a qualitative analysis via semi-structured interviews is examining the feasibility, sustainability, and potential lifestyle changes associated with the implementation of packaged FMDs for male health. The counterpart of the study, using a prolonged fast on female subfertile patients, showed difficulties in recruitment. Why fasting was so difficult to implement in the setting of fertility clinics is the objective of yet another qualitative study that was presented by Ms. Batschari (Charité—Universitätsmedizin Berlin).

2.5 Practical Aspects in Broad Clinical Application

Applying fasting in larger settings and making it available to more and more people in hospitals and outpatient services engenders challenges that were addressed in two panel discussions during the conference.

The first of two panel discussions dealt with the feasibility of fasting in everyday clinical practice. Prof. Michalsen (Charité—Universitätsmedizin Berlin, ÄGHE Board member), Dr. Matejka (Malteser Klinik von Weckberger, ÄGHE Board member), Dr. Ritzmann-Widderich (Medical Office in Rottweil, Germany, ÄGHE Board member), Dr. Sartor (Sigmund Freud University Vienna, Austria, LANSMED Akademy, Biovis Diagnostiks MVZ GmbH, Upgraders®) and Ms. Rajput Khokhar (Charité—Universitätsmedizin Berlin, ÄGHE Board member) discussed frequently asked questions of patients regarding the consumption of coffee and the intake of salt as well as the necessity, advantages and disadvantages of bowel cleansing methods during the fasting intervention. The results of the discussion are shown in Table 1.

The second panel discussion focused on the implementation of fasting in the outpatient setting, since therapeutic fasting has not yet been widely used there. The panel, composed of various educational institutions, examined the questions of whether and how fasting can be made accessible to the general public and what is needed for its safe and effective implementation. A good infrastructure already exists with regard to preventive fasting in the outpatient sector in German speaking countries. To become a fasting coach, trained by the German Fasting Academy (Deutsche Fastenakademiee.V., dfa) or the Association for Independent Health Counseling (Verband für Unabhängige Gesundheitsberatung, UGB) among others, no medical profession is required. Medical and nutritional expertise on the other hand, to apply fasting as a therapeutic intervention, is underdeveloped. The dfa, UGB, Academy of Integrative Fasting (Akademie für Integratives Fasten, AIF) and the ÄGHE therefore discussed possible synergies and necessary training opportunities. The discussion showed that synergies already exist, for example, trained fasting coaches could offer therapeutic fasting weeks with the support of trained physicians. In order to achieve this, more physicians need to be trained, especially on the necessities of fasting in the outpatient setting, in particular regarding indications, contraindications and adaptation of medications. Furthermore, everyone involved (fasting coaches, physicians, person that is fasting) should be aware of the great potential of fasting with regard to sustainable behavioral changes (diet, lifestyle, etc.) in the long-term.

3 Summary

The conference and the preceding symposium included presentations and discussions on various fasting methods from different research fields, resulting in a productive and stimulating meeting for researchers and clinicians alike. The multitude of contributions made the achievements already obtained and the questions to be studied more evident. A lot has been accomplished regarding the exploration of TRE in metabolic indications, and good, although still sparse, evidence has been collected in oncology. The effects of various fasting diets on the gut microbiome and immune system are currently being studied, and the field and its implications are vast. Gender differences in response to fasting, as well as psychological, behavioral, and health aspects, remain to be investigated. Including religious fasts in the discussion could help understand motivational and subjective aspects of fasting and their impact on individual and public health. Finally, although the experimental data on fasting are extensive, several subsets of cellular and organ responses remain to be described in more detail. Last but not least, new technologies hold high promises of assisting clinical fasting research and practice.

CONFLICTS OF INTEREST STATEMENT

AM, EH, ARK and DK are members of the steering committee of the ÄGHE. AM and DK have co-founded the Academy of Integrative Fasting (AIF), an institution for the qualification of medical staff in clinical fasting applications. AM is also Co-founder of the SALUFAST company and DK serves as a consultant for a mobile application on intermittent fasting (FASTIC) as well as a company producing plant-based supplements (EVERYYIN). All other authors declare no conflict of interest related to this manuscript.

FUNDING SOURCES

The event was made possible thanks to the support of the *EDEN* Foundation, the *Software AG* Foundation and the *Karl und Veronica Carstens* Foundation as well as the sponsors:
Akademie für Integratives Fasten GbR
BIOMES
biovis Diagnostik
BitterKraft
BKK VBU Betriebskrankenkasse
Deutsche Fastenakademie e.V.
GANZIMMUN Diagnostics GmbH
IMD Institut für Medizinische Diagnostik Berlin-Potsdam GbR
Institut AllergoSan GmbH
Klinik Buchinger Wilhelmi
Kurpark-Klinik
Lanserhof
Luvos
Malteser-Klinik Dr. von Weckbecker gGmbH
Moleqlar

mybioma
Norsan
Prolon
ProtinaPharmazeutische GmbH
Salufast
Schloss Warnsdorf Klinik
Startkraft GmbH
Verband für Unabhängige Gesundheitsberatung e.V. (UGB)

AUTHOR CONTRIBUTIONS
Took a major part in planning the conference and symposium (CB, SM, EH, SJ, MB, ARK, AM, DK); Summarized all contributions (CB, SM, EH, SJ, MB, ARK, DK); Wrote the paper (ALL AUTHORS)

References

1. Wilhelmi de Toledo F, Grundler F, Sirtori CR, Ruscica M. Unravelling the health effects of fasting: a long road from obesity treatment to healthy life span increase and improved cognition. Annals of Medicine. 2020;52(5):147-61.
2. Albosta M, Bakke J. Intermittent fasting: is there a role in the treatment of diabetes? A review of the literature and guide for primary care physicians. Clin Diabetes Endocrinol. 2021;7(1):3.
3. Tiwari S, Sapkota N, Han Z. Effect of fasting on cancer: A narrative review of scientific evidence. Cancer Sci. 2022;113(10):3291-302.
4. Thürmer M, Gollowitzer A, Pein H, Neukirch K, Gelmez E, Waltl L, et al. PI(18:1/18:1) is a SCD1-derived lipokine that limits stress signaling. Nature Communications. 2022;13(1):2982.
5. Kiechl S, Pechlaner R, Willeit P, Notdurfter M, Paulweber B, Willeit K, et al. Higher spermidine intake is linked to lower mortality: a prospective population-based study. Am J Clin Nutr. 2018;108(2):371-80.
6. Schroeder S, Hofer SJ, Zimmermann A, Pechlaner R, Dammbrueck C, Pendl T, et al. Dietary spermidine improves cognitive function. Cell Rep. 2021;35(2):108985.
7. Eisenberg T, Abdellatif M, Schroeder S, Primessnig U, Stekovic S, Pendl T, et al. Cardioprotection and lifespan extension by the natural polyamine spermidine. Nat Med. 2016;22(12):1428-38.
8. Liang Y, Piao C, Beuschel CB, Toppe D, Kollipara L, Bogdanow B, et al. eIF5A hypusination, boosted by dietary spermidine, protects from premature brain aging and mitochondrial dysfunction. Cell Rep. 2021;35(2):108941.
9. Madeo F, Eisenberg T, Pietrocola F, Kroemer G. Spermidine in health and disease. Science. 2018;359(6374).
10. Schwarz C, Stekovic S, Wirth M, Benson G, Royer P, Sigrist SJ, et al. Safety and tolerability of spermidine supplementation in mice and older adults with subjective cognitive decline. Aging (Albany NY). 2018;10(1):19-33.
11. Manlik T, Pivovarova-Ramich O, Pappe C, Liebscher D, Arnrich B, Steckhan N. Fasting state prediction using continuous glucose monitoring, activity and nutritional data: a tool for compliance evaluation in remote fasting trials2023.
12. Moro T, Tinsley G, Bianco A, Marcolin G, Pacelli QF, Battaglia G, et al. Effects of eight weeks of time-restricted feeding (16/8) on basal metabolism, maximal strength, body composition, inflammation, and cardiovascular risk factors in resistance-trained males. J Transl Med. 2016;14(1):290.
13. Tovar AP, Richardson CE, Keim NL, Van Loan MD, Davis BA, Casazza GA. Four Weeks of 16/8 Time Restrictive Feeding in Endurance Trained Male Runners Decreases Fat Mass, without Affecting Exercise Performance. Nutrients. 2021;13(9).
14. Moro T, Tinsley G, Longo G, Grigoletto D, Bianco A, Ferraris C, et al. Time-restricted eating effects on performance, immune function, and body composition in elite cyclists: a randomized controlled trial. J Int Soc Sports Nutr. 2020;17(1):65.
15. Kotarsky CJ, Johnson NR, Mahoney SJ, Mitchell SL, Schimek RL, Stastny SN, et al. Time-restricted eating and concurrent exercise training reduces fat mass and increases lean mass in overweight and obese adults. Physiol Rep. 2021;9(10):e14868.
16. Persynaki A, Karras S, Pichard C. Unraveling the metabolic health benefits of fasting related to religious beliefs: A narrative review. Nutrition. 2017;35:14-20.

17. Ring RM, Eisenmann C, Kandil FI, Steckhan N, Demmrich S, Klatte C, et al. Mental and Behavioural Responses to Bahá'í Fasting: Looking behind the Scenes of a Religiously Motivated Intermittent Fast Using a Mixed Methods Approach. Nutrients. 2022;14(5).
18. Lin S, Cienfuegos S, Ezpeleta M, Gabel K, Pavlou V, Mulas A, et al. Time-Restricted Eating Without Calorie Counting for Weight Loss in a Racially Diverse Population : A Randomized Controlled Trial. Ann Intern Med. 2023;176(7):885-95.
19. Varady KA, Cienfuegos S, Ezpeleta M, Gabel K. Clinical application of intermittent fasting for weight loss: progress and future directions. Nat Rev Endocrinol. 2022;18(5):309-21.
20. Peters B, Koppold-Liebscher DA, Schuppelius B, Steckhan N, Pfeiffer AFH, Kramer A, et al. Effects of Early vs. Late Time-Restricted Eating on Cardiometabolic Health, Inflammation, and Sleep in Overweight and Obese Women: A Study Protocol for the ChronoFast Trial. Front Nutr. 2021;8:765543.
21. Salvadori G, Zanardi F, Iannelli F, Lobefaro R, Vernieri C, Longo VD. Fasting-mimicking diet blocks triple-negative breast cancer and cancer stem cell escape. Cell Metab. 2021;33(11):2247-59.e6.
22. Vernieri C, Fucà G, Ligorio F, Huber V, Vingiani A, Iannelli F, et al. Fasting-Mimicking Diet Is Safe and Reshapes Metabolism and Antitumor Immunity in Patients with Cancer. Cancer Discov. 2022;12(1):90-107.
23. Baruch EN, Gaglani T, Wargo JA. Fecal microbiota transplantation as a mean of overcoming immunotherapy-resistant cancers - hype or hope? Ther Adv Med Oncol. 2021;13:17588359211045853.
24. Davar D, Dzutsev AK, McCulloch JA, Rodrigues RR, Chauvin JM, Morrison RM, et al. Fecal microbiota transplant overcomes resistance to anti-PD-1 therapy in melanoma patients. Science. 2021;371(6529):595-602.
25. Schmidt M, Brenner W, Gebhard S, Schmidt M, Singer S, Weidenbach L, et al. Effects of intermittent fasting on quality of life tolerance of chemotherapy in patients with gynecological cancers: study protocol of a randomized-controlled multi-center trial. Frontiers in Oncology. 2023;13.
26. Jordan S, Tung N, Casanova-Acebes M, Chang C, Cantoni C, Zhang D, et al. Dietary Intake Regulates the Circulating Inflammatory Monocyte Pool. Cell. 2019;178(5):1102-14.e17.
27. Hansen B, Laczny CC, Aho VTE, Frachet-Bour A, Habier J, Ostaszewski M, et al. Protocol for a multicentre cross-sectional, longitudinal ambulatory clinical trial in rheumatoid arthritis and Parkinson's disease patients analysing the relation between the gut microbiome, fasting and immune status in Germany (ExpoBiome). BMJ Open. 2023;13(8):e071380.
28. Koppold DA, Kandil FI, Güttler O, Müller A, Steckhan N, Meiß S, et al. Effects of Prolonged Fasting during Inpatient Multimodal Treatment on Pain and Functional Parameters in Knee and Hip Osteoarthritis: A Prospective Exploratory Observational Study. Nutrients. 2023;15(12):2695.
29. Papagiannopoulos-Vatopaidinos IE, Papagiannopoulou M, Sideris V. Dry Fasting Physiology: Responses to Hypovolemia and Hypertonicity. Complement Med Res. 2020;27(4):242-51.
30. Papagiannopoulos IA, Sideris VI, Boschmann M, Koutsoni OS, Dotsika EN. Anthropometric, hemodynamic, metabolic, and renal responses during 5 days of food and water deprivation. Forsch Komplementmed. 2013;20(6):427-33.
31. Mesnage R, Grundler F, Schwiertz A, Le Maho Y, Wilhelmi de Toledo F. Changes in human gut microbiota composition are linked to the energy metabolic switch during 10 d of Buchinger fasting. Journal of Nutritional Science. 2019;8:e36.

Table 1: Summary of Expert recommendations from the Panel Discussion

FAQs on Prolonged Fasting	**Expert recommendations**
Coffee	- Stepwise reduction of caffeine intake a week before prolonged fasting to prevent headaches. - For headaches during the first 2 days of fasting in coffee drinkers, an espresso might help. - Coffee consumption is generally not advised during fasting (may cause palpitations and increase sweating).
Salt (NaCl)	- In hypertensive patients, salt reduction should be maintained as in traditional fasting traditions. - Athletes, people with underweight and patients with a long history of diuretics could benefit from an additional intake of salt during fasting to prevent hyponatremia. - Patients suffering from symptomatic low blood pressure can profit from additional salt intake during fasting.
Laxatives	- Necessity: Differing opinions worldwide - Laxation could have a positive influence on the fasting process, but magnesium and sodium sulphate or hydrocolon therapy are not suitable for everyone. For people with sensitive or weak circulation, enemas, castor oil or sauerkraut juice may be more suitable.