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Impact of dairy intake on circulating fatty acids and associations with blood pressure: A randomized crossover trial

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ABSTRACT

Background and aims: This study aimed to investigate the effects of high and adequate dairy intake (>4, 2–3 serving/day, respectively) on circulating fatty acids (FAs) and their associations with blood pressure (BP).
Methods and results: A randomized crossover clinical trial was conducted with 27 participants (8 women, 19 men) at the CHU de Québec-Université Laval Research Center. Participants were assigned to either a high-dairy (HD) or adequate-dairy (AD) diet for six weeks, followed by a six-week washout period before crossing over. Plasma phospholipid-bound FAs were analyzed using gas chromatography, and BP and arterial stiffness were measured at each visit. Partial correlation analyses, generalized linear mixed models and machine learning techniques were employed to analyze the data.
Pentadecanoic acid (15:0) and heptadecanoic acid (17:0) were positively correlated with dairy intake and showed increases after the HD. Palmitic acid (16:0) and total saturated FAs were positively associated with systolic (SBP) and diastolic (DBP), while 17:0 was inversely associated with diastolic BP.
Conclusions: HD was associated with increased 15:0 and 17:0. Notably, 17:0 had an inverse association with diastolic BP, while 16:0 was positively linked. These findings highlight the importance of dietary strategies that incorporate specific FAs to enhance cardiovascular health. Registration number: NCT02961179.

1. Introduction

Fatty acids (FAs) are essential substrates for the synthesis of endocrine mediators, which are involved in key biological functions, including inflammatory processes and cardiovascular regulation [1]. The FA profile represents the composition and concentration of specific FAs in biological samples such as tissues, blood, or lipid extracts [2]. FA levels in the bloodstream are modified by both dietary fat intake and endogenous metabolism [3]. Blood FAs can modulate vascular inflammation, vascular tone, impacting blood pressure (BP) and arterial stiffness [4–7].

In Canada, approximately 24 % of adults have hypertension (HTN), commonly known as high systolic (>140 mmHg) and/or diastolic (>90 mmHg) BP [8]. Individuals with diabetes are at nearly double risk for cardiovascular disease (CVD) including HTN [9]. Insulin resistance and hyperglycemia contribute to HTN and arterial stiffness in type 2 diabetes (T2D) by promoting chronic inflammation, oxidative stress, impaired vasodilation, increased angiotensin II levels, and reduced nitric oxide production, which together exacerbate endothelial dysfunction and lead to atherosclerosis [10–17]. A cross-sectional study found that hypertensive individuals had higher levels of saturated (myristic (14:0), palmitic (16:0), stearic (18:0), behenic (22:0) acids) and monounsaturated FAs (MUFAs) (palmitoleic (16:1*n*7), oleic (18:1*n*9) acids), along with gamma-linolenic acid (18:3*n*6), and dihomo-gamma-linolenic acid

Abbreviations: FAs, fatty acids; BP, blood pressure; HD, high-dairy; AD, adequate-dairy; HOMA-IR, Homeostatic Model Assessment of Insulin Resistance; LDL, Low-Density Lipoprotein; HTN, hypertension; CVD, cardiovascular disease; T2D, type 2 diabetes; MUFAs, monounsaturated FAs; PUFAs, polyunsaturated FAs; SFAs, saturated FAs; ALA, alpha-linolenic acids; VLSFAs, Very-long-chain SFAs; SBP, systolic; DBP, diastolic; BMI, body mass index; HbA1c, glycated hemoglobin; FPG, fasting plasma glucose; FFQ, food frequency questionnaires; cfPWV, carotid-femoral pulse wave velocity; GLMM, generalized linear mixed models; RFE, recursive feature elimination; LASSO, least absolute shrinkage and selection operator; VIF, variance inflation factor; KNN, K-Nearest Neighbors; SVM, Support Vector Machine; ANN, Artificial Neural Network; bSBP, brachial SBP; cSBP, central SBP; cMAP, central mean arterial pressure; AP, augmentation pressure; AIx, augmentation index.

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(20:3*n*6). In contrast, hypertensive individuals had lower levels of linoleic (18:2*n*6) and docosahexaenoic acid (22:6*n*3), *n*3 polyunsaturated FAs (PUFAs), PUFAs, and a lower *n*3/*n*6 ratio, while showing higher saturated FAs (SFAs) and SFA/PUFA ratios compared to normotensive participants [18]. Similarly, a cohort study linked higher myristic (14:0) and arachidonic acid (20:4*n*6) levels with an increased risk of T2D, while petroselinic (18:1*n*12) and alpha-linolenic acids (ALA) were associated with reduced T2D risk [19]. Very-long-chain SFAs (VLSFAs) (arachidic (20:0), behenic (22:0), and lignoceric acid (24:0)) were also associated with a lower risk of T2D in participants at-risk of diabetes [20]. Another cohort study found that higher plasma SFAs and MUFA levels increased T2D risk, while higher PUFA, n-6, and n-3 PUFAs were protective [3]. Together, these studies suggest that specific FAs profiles are associated with BP and T2D.

Specific circulating FAs, including palmitoleic acid (*trans*-16:1*n*7), heptadecanoic acid (17:0), pentadecanoic acid (15:0), and myristic acid (14:0), are primarily associated with dairy fat consumption [21]. Previous studies have consistently demonstrated a positive relationship between dairy intake and plasma levels of 15:0 and 17:0 [22,23]. A study reported an inverse association between serum 15:0 levels and elevated BP [24]. Additionally, two observational studies in adults found a positive relationship between 16:1*n*7 and both systolic (SBP) and diastolic (DBP) [24,25]. Further, a systematic review and meta-analysis confirmed that odd-chain SFAs 15:0 and 17:0 have a protective effect against T2D [26]. Conversely, the even-chain SFA 14:0 was associated with an increased risk of T2D [26].

Collectively, these studies suggest that dairy intake may influence circulating FAs, which are also associated with BP. However, there is a lack of research exploring both dairy-induced and other circulating FAs in relation to BP and arterial stiffness, a factor modulating BP, in individuals at risk of T2D. Therefore, the objective of this manuscript is to investigate the effects of high dairy intake (>4 servings/day) compared to adequate dairy intake (2–3 servings/day) on circulating FAs and their associations with BP in subjects with hyperinsulinemia. The primary objective of the overall study was to investigate the change from baseline to 6 weeks of high dairy (HD) intake (>4 servings/day) compared to adequate dairy (AD) intake (2–3 servings/day) on insulin sensitivity [27] in hyperinsulinemic adults. One of the secondary outcomes was to investigate changes in plasma FA concentrations resulting from HD intake compared to AD intake [28]. Further, in the current study, the role of FAs as biomarkers for dairy intake and contributors to BP regulation was examined.

2. Materials

The current study constitutes an examination of secondary outcomes using data obtained from the primary study of a randomized crossover clinical trial (NCT02961179) at the CHU de Québec-Université Laval Research Center [27].

2.1. Study population

This study was based on previous work [29–31]. Between February 2017 and July 2018, participants were recruited for a randomized crossover clinical trial (NCT02961179) at the CHU de Québec-Université Laval Research Center. Recruitment methods included poster advertisements, flyers, and email lists from the Institute of Nutrition and Functional Foods and Université Laval.

Eligible participants were Caucasian men and postmenopausal women (with no menstrual cycles for over 12 months), aged 18 years or older, with a body mass index (BMI) between 25 and 40 kg/m^2. Participants had to have a stable body weight (no more than 5 % variation in the three months before screening), glycated hemoglobin (HbA1c) below 6.5 % (47 mmol/mol), fasting insulin levels above 90 pmol/L, and fasting plasma glucose (FPG) levels below 7.0 mmol/L. Exclusion criteria included high dairy consumption (more than two servings per day), allergies, aversions, or intolerance to dairy products, smoking, T2D or other disorders related to glucose metabolism, inflammatory bowel disease, or any gastrointestinal disorder affecting digestion or nutrient absorption. Additionally, individuals on medications that impact lipid or glucose metabolism were excluded. All participants provided written informed consent prior to the intervention. Participants deemed eligible through telephone screening were invited for a screening visit, where they completed demographic, medical, and food frequency questionnaires (FFQ).

The study adhered to the principles of the Helsinki Declaration and received approval from the CHU de Québec-Université Laval Research Center ethics committees (permission code: 2017–3228). The trial protocol is registered on ClinicalTrials.gov under the identifier NCT02961179.

2.2. Dietary intervention

Participants were randomly assigned to either a high-dairy (HD) or adequate-dairy (AD) (1:1) diet for six weeks, followed by a six-week washout period before crossing over to the alternate diet for another six weeks. Random assignment was facilitated by a computer-generated sequence using blocks of 10 participants, with no concealment of allocation.

During the HD intervention, participants consumed at least four servings of dairy daily, substituting other foods to avoid weight gain. In the AD intervention, participants consumed 2–3 servings per day, following Canada's Food Guide (2007), while maintaining their usual diet, activity, and lifestyle.

Dairy products included cheese, kefir, milk, yogurt, and cream (up to 15 % fat). Ice cream was limited to three 125 ml servings per week, and high-fat options like whipped cream and butter were excluded. A registered dietitian provided serving instructions. In the HD phase, participants were advised to consume more than four servings daily, with dairy products and financial compensation provided.

Dietary intake was monitored using a validated FFQ with 91 items and 33 sub questions, administered through a nutrition-related web platform [32]. Intake data were analyzed using the Canadian Nutrient File 2015. During the washout period, participants were asked to return to their regular dairy consumption of two or fewer servings per day. To enhance the accuracy of dietary monitoring, three randomly timed 24-h dietary recalls were conducted during each intervention phase. These recalls provided more detailed, day-to-day dietary data, which were used to cross-validate the FFQ data for consistency and accuracy in reporting total energy intake. Monitor adherence to dietary intervention and ensure participants met the target dairy intake for each phase. This combined approach of FFQ and 24-h recalls ensured robust dietary monitoring throughout the study.

2.3. Blood pressure and arterial stiffness

Detailed information regarding anthropometric measurements, biochemical measurements, and assessments of hemodynamic and arterial stiffness can be found in previously published studies [29–31]. BP and arterial stiffness were assessed using the SphygmoCor® XCEL system (AtCor Medical, Sydney, Australia) after 15 min of rest, with participants seated for BP and supine for PWV. Brachial BP and central pressures were measured on the right arm, using an appropriate cuff size, and the average of two high-quality measurements was used for analysis. Carotid-femoral pulse wave velocity (cfPWV) was recorded twice via applanation tonometry, with distances calculated per manufacturer guidelines. Measurements were averaged and verified for quality, conducted by the same trained assistant at consistent times [29].

2.4. Plasma phospholipid-bound fatty acid measurements

Plasma lipids were spiked with phosphatidylcholine 21:0 as an internal standard, as previously described [33]. Briefly, lipids were extracted using a chloroform-methanol mixture (2:1 v/v) following a modified Folch method [34]. Phospholipids were then isolated via thin-layer chromatography using a solvent combination of isopropyl ether and acetic acid (96:4, by volume). FAs from these phospholipids were methylated using methanol/benzene mixture (4:1, by volume) and acetyl chloride at 95 °C for 1.5 h [35]. The methylated FAs were analyzed by capillary gas chromatography on a HP5890 gas chromatograph (Hewlett Packard, Toronto, Canada), equipped with an HP-88 capillary column (100 m × 0.25 mm internal diameter × 0.20 μm film thickness; Agilent Technologies, Oakville, Ontario, Canada) and a flame ionization detector. Helium was used as the carrier gas with a split ratio of 1:50. Fatty acid identification was accomplished by comparing their retention times to those of standard mixtures, including the FAME 37 mix (Supelco Inc., Bellefonte, PA), the GLC411 FA mix (NuChek Prep Inc., Elysian, MN), methylated FA 22:5n-6 (Larodan AB, Malmö, Sweden), and 22:5n-3 (Supelco Inc., Bellefonte, PA). Additionally, a standard mixture containing various *trans*-FA and isoforms of 18:1 was used, sourced from NuChek Prep Inc. and Supelco Inc. The FAs results were presented as a percentage of the total FAs.

2.5. Statistical analysis

The differences in FAs before and after the interventions (pre-post AD, pre-post HD, pre-AD and pre-HD, post-AD and post-HD) were analyzed using generalized linear mixed models (GLMM). The GLMM procedure included a repeated statement (visits 1, 2, 3, and 4, or phase (pre-post)) and a covariance structure that minimized the Akaike criterion. A random-intercept model for each subject provided the best fit. Fixed effects for the GLMM analyses of pre-post AD and pre-post HD included BMI, sex, age, phase*order, and order; for post-AD and post-HD, the fixed effects included BMI, sex, age, order, and the interaction between order and intervention. Bonferroni correction was applied to the models. To achieve normality, data were logarithmically transformed using gamma regression distribution. Partial correlation analysis was used to assess the relationships between dairy intake and phospholipid-derived FAs, adjusted for sex, BMI, age, visit number, intervention, and order. Additionally, partial correlation analysis, combining data from all four visits, was used to evaluate the relationships between BP and arterial stiffness markers with phospholipid-derived FAs, adjusted for sex, BMI, age, visit number, intervention, order, and dairy intake.

Machine learning techniques were employed to develop a model to predict high BP. Feature selection was performed using recursive feature elimination (RFE), least absolute shrinkage and selection operator (LASSO), and tree-based feature selection. To ensure multicollinearity was not an issue, the variance inflation factor (VIF) was calculated for each feature, and all features had a VIF of less than 5. The features were standardized using Python StandardScaler function.

The models evaluated in this study included Naive Bayes, K-Nearest Neighbors (KNN), Support Vector Machine (SVM), Logistic Regression, Random Forest, and Artificial Neural Network (ANN). Each model was assessed using 10-fold cross-validation to compute accuracy, precision, recall, and F1-score using Python.

Accuracy measures the overall correctness of the model by calculating the ratio of correctly predicted instances to the total instances. It is given by the formula:

$$\text{Accuracy} = (\text{True Positives} + \text{True Negatives}) / \text{Total Instances}$$

Precision assesses the accuracy of the positive predictions by calculating the ratio of true positive instances to the total instances that were predicted as positive. It is given by the formula:

$$\text{Precision} = \text{True Positives} / (\text{True Positives} + \text{False Positives})$$

Recall measures the model's ability to correctly identify all relevant instances by calculating the ratio of true positive instances to the total actual positive instances. It is given by the formula:

$$\text{Recall} = \text{True Positives} / (\text{True Positives} + \text{False Negatives})$$

F1-score is the harmonic means of precision and recall, providing a single score that balances both the concerns of precision and recall. It is given by the formula:

$$\text{F1-score} = 2 * (\text{Precision} * \text{Recall}) / (\text{Precision} + \text{Recall})$$

To identify the optimal parameters for the Random Forest and KNN models, the Random Forest model was evaluated with n_estimators set to 10, 50, 100, and 200, while the KNN model was tested with n_neighbors set to 3, 5, 7, 9, and 11.

A post hoc sample size calculation was conducted to determine whether the study was adequately powered to detect the observed effect of dairy intake on circulating 15:0, biomarkers of dairy products [36], levels in this randomized crossover trial. Since each participant served as their own control, a paired *t*-test approach was used to estimate the required sample size.

The required sample size was calculated using the following formula [37]:

$$n = (Z\alpha / 2 + Z\beta)\hat{2} \times 2\sigma^2 \; / \; d^2$$

where.

- $Z\alpha/2 = 1.96$ (two-tailed test, $\alpha = 0.05$)
- $Z\beta = 0.84$ (80 % power)
- $\sigma^2 = 0.001640$ (pooled within-subject variance from pre- and post-values)
- $d = 0.032$ (mean difference in 15:0 pre-post intervention)

Using this approach, the required sample size was 26 participants, indicating that the study had sufficient power to detect the observed effect.

Statistical significance was defined as $p \leq 0.05$. Data analysis was performed using IBM SPSS Statistics 26 for Microsoft Windows (IBM Corp., Armonk, NY, USA) and Python version 3.11.4.

3. Results

3.1. Participant characteristics

Twenty-seven participants (8 women, 19 men) completed the study. Baseline characteristics are presented in Table 1, stratified by the randomized order of intervention: AD followed by HD (n = 15) and HD followed by AD (n = 12). Participants in the HD/AD group had significantly lower baseline diastolic blood pressure compared to those in the AD/HD group ($p = 0.021$). The overall baseline mean values for all participants were as follows: age, 55.4 ± 14 years; BMI, 31.4 ± 3.2 kg/m^2; SBP, 137 ± 12 mmHg; and DBP, 79 ± 10 mmHg. Following the HD phase, participants consumed more dairy products ($P < 0.01$, 95 % CI: 2.46 to 4.10), accompanied by increased intake of protein ($P < 0.01$, 95 % CI: 7.95 to 34.56) and saturated fatty acids (SFA) ($P = 0.01$, 95 % CI: 1.53 to 12.85) at week 6 compared to baseline. Furthermore, participants in the HD phase consumed more full-fat ($P < 0.01$, 95 % CI: 0.30 to 1.80) and low-fat dairy products ($P < 0.01$, 95 % CI: 1.80 to 3.30) compared to both baseline and the AD phase. No other significant differences including fiber intake, were observed between intervention phases. Weight stability was a key indicator of controlled energy intake during the intervention. Participants were instructed to substitute dairy products for other foods in their diet rather than increase total energy intake. Body weight was monitored throughout the study to ensure

Table 1
Subject characteristics at the baseline.

Characteristics	AD/HD (Mean ± SD) N = 15	HD/AD (Mean ± SD) N = 12	P *
Biological sex (male/female)	12/3	7/5	0.236
Age, year	55.60 ± 14.18	55.35 ± 14.42	0.964
Body weight, kg	91.5 ± 15.9	88.7 ± 14.4	0.905
BMI, kg/m2	31.21 ± 3.25	31.50 ± 3.22	0.981
Waist circumference, cm	109.49 ± 7.87	108.44 ± 10.31	0.867
Systolic blood pressure, mm Hg	135.6 ± 10.5	137 ± 13.2	0.829
Diastolic blood pressure, mm Hg	85.6 ± 9.2	76.8 ± 9	0.021
Body fat mass, kg	30.3 ± 8.7	31.8 ± 8.2	0.548
Lean body mass, kg	61.7 ± 12.8	57.4 ± 12.9	0.347
Lean dry mass, kg	16.4 ± 3.5	15.3 ± 3.5	0.399
Total body water	45.3 ± 9.4	42.1 ± 9.4	0.323
Serum fasting glucose, mmol/L	5.21 ± 0.54	5.36 ± 0.38	0.399
Serum fasting insulin, pmol/L	109 ± 46	124 ± 60	0.519
Insulin resistance, HOMA-IR	4.17 ± 1.48	4.99 ± 2.80	0.340
HDL, mmol/L	1.07 ± 0.23	1.14 ± 0.24	0.399
LDL, mmol/L	2.55 ± 0.62	2.77 ± 1.10	0.516
Total cholesterol, mmol/L	4.37 ± 0.82	4.71 ± 1.21	0.548
cfPWV, m/sec	8 ± 1	7 ± 1	0.734
Central systolic pressure, mm Hg	123.8 ± 10.3	122.3 ± 13.2	0.516
Central diastolic pressure, mm Hg	86.1 ± 9.2	77.6 ± 8.9	0.021
Central pulse pressure, mm Hg	37.6 ± 6.1	44.6 ± 12.1	0.087
Mean arterial pressure	100.4 ± 9.2	94.8 ± 8.9	0.152
Central augmentation pressure	9.9 ± 5.7	10.8 ± 7.7	0.792
AIx, %	24.9 ± 13.4	23 ± 13.9	0.581

n = 27, Values were presented as mean ± SD. * Comparison between groups was performed using Independent *t*-test and Mann-Whitney U. P < 0.05 was considered significant. AD, adequate dairy product intake; HD, high dairy product intake; BMI, body mass index; HDL, high-density lipoprotein; LDL, low-density lipoprotein; cfPWV, carotid-femoral pulse wave velocity; AIx normalized for heart rate of 75 bpm.

compliance with this guideline, and significant changes in weight were considered indicative of deviations in energy balance. As reported in the original study [27], no differences in weight were observed between intervention phases, suggesting that energy intake was effectively controlled. Additionally, reported energy intake (kcal) did not differ between the HD and AD phases, further supporting the maintenance of energy balance (results not shown).

3.2. Fatty acids and dairy intake

A GLMM model with random intercepts was employed to assess the differences in phospholipid FAs before and after the AD and HD interventions, as presented in Table 2. The FAs 14:0, 15:0, 16:0, 17:0, dihomo-gamma-linolenic acid (20:3*n*6), 22:5*n*3, and SFAs showed differences between the post-AD and post-HD periods, with higher levels observed after HD ($p < 0.05$). Conversely, the FAs 20:1*n*9, 22:0, ($\sum n3 + \sum n6$)/SFAs, $\sum cis$ FAs, $\sum n6$ FAs, PUFAs, and $\sum cis$ *n*6 FAs were also different between the post-AD and post-HD periods but exhibited lower levels after HD, with decreases observed post-HD ($p < 0.05$).

The partial correlations between FAs and total dairy intake are shown in Table 3. To evaluate the correlation between FAs and dairy intake, data from all four visits were combined. The correlations were adjusted for sex, BMI, age, visit number, intervention, and order. The FAs 15:0 and 17:0 (r = 0.364, 0.321; p < 0.001, 0.001) were positively correlated with dairy intake, while 18:0 and 22:6*n*3 (r = −0.208, −0.195; p = 0.036, 0.049) were negatively correlated with dairy intake.

3.3. Fatty acids and blood pressure

The partial correlations between FAs and hemodynamic parameters, combining data from all four visits, are shown in Table 4. The correlations were adjusted for sex, BMI, age, visit number, intervention, order, and dairy intake. The 16:0 was positively correlated with brachial SBP (bSBP), bDBP, central SBP (cSBP), cDBP, and central mean arterial pressure (cMAP) (r = 0.238, 0.327, 0.279, 0.328, 0.289; p = 0.035, 0.003, 0.013, 0.003, 0.01 respectively). SFAs were positively correlated with bSBP, bDBP, cSBP, cDBP, cMAP, augmentation pressure (AP), augmentation index (AIx), and carotid-femoral pulse wave velocity (cfPWV) (r = 0.391, 0.373, 0.461, 0.383, 0.417, 0.321, 0.263, 0.278; p = <0.001, 0.001, <0.001, <0.001, <0.001, 0.004, 0.019, 0.013 respectively). Conversely, 17:0 was negatively correlated with bDBP, cDBP, and cMAP (r = −0.234, −0.244, −0.233; p = 0.038, 0.03, 0.039). Additionally, ($\sum n3 + \sum n6$)/SFAs, and $\sum cis$ FAs were negatively correlated with bSBP, bDBP, cSBP, cDBP, cMAP, AP, and AIx (r = −0.386, −0.343, −0.463, −0.351, −0.380, −0.407, −0.343; p = <0.001, 0.002, <0.001, 0.001, 0.001, <0.001, 0.002) (r = −0.415, −0.381, −0.495, −0.392, −0.434, −0.369, −0.307; p = <0.001, 0.001, <0.001, <0.001, <0.001, 0.001, 0.006). Total *cis* FAs was also negatively correlated with cfPWV (r = −0.260; p = 0.021).

The machine learning models for predicting HTN, which incorporate clinical parameters and FAs data from all four visits, are presented in Tables 5abc.

3.4. Predictive models using fatty acids data

The predictive models for high SBP (≥140 mmHg) and DBP (≥90 mmHg) using FAs data from all four visits are presented in Table 5a. The features used in the models were 9*c*-16:1*n*7, 20:0, 18:3*n*6, 18:4*n*3, and 22:5*n*3. The performance metrics for each model, including accuracy, precision, recall, and F1-score, are detailed below.

For predicting high SBP, the SVM model demonstrated the best performance with an accuracy of 0.687, precision of 0.703, recall of 0.916, and an F1-score of 0.794. For predicting high DBP, the KNN, SVM, and Logistic Regression models all showed excellent performance, each with an accuracy of 0.815, precision of 0.815, recall of 1.000, and an F1-score of 0.898 respectively.

3.5. Predictive models using clinical parameters

The predictive models for high SBP and DBP using clinical parameters from all four visits are presented in Table 5b. The features used in the models included waist circumference, homeostatic model assessment of insulin resistance (HOMA-IR), low-density lipoprotein (LDL), and age.

For predicting high SBP, the KNN model demonstrated the best performance with the accuracy of 0.817, precision of 0.843, recall of 0.902, and an F1-score of 0.865. For predicting high DBP, the KNN model showed the highest performance with the accuracy of 0.852, precision of 0.880, recall of 0.954, and an F1-score of 0.865 respectively.

3.6. Predictive models using clinical parameters and fatty acids data

The predictive models for high SBP and DBP using clinical parameters and FAs data from all four visits are presented in Table 5c. The features used in the models included waist circumference, homeostatic model assessment of insulin resistance (HOMA-IR), low-density lipoprotein (LDL), age, 16:1*n*7, 20:0, and 20:3*n*6. The performance metrics for each model, including accuracy, precision, recall, and F1-score, are detailed below.

To predict high SBP, the SVM model demonstrated the best performance with the accuracy of 0.770, precision of 0.790, recall of 0.902, and an F1-score of 0.837. For predicting high DBP, the KNN model showed the highest performance with the accuracy of 0.872, precision of 0.900, recall of 0.956, and an F1-score of 0.925 respectively.

4. Discussion

Results demonstrate a positive correlation between odd-chain FAs 15:0 and 17:0 with dairy intake. Further differences were observed in

Table 2
Differences in phospholipid derived fatty acids before and after the interventions.

Fatty Acid	Pre-AD Mean ± SD	Post-AD Mean ± SD	p-value[a] (AD)	Pre-HD Mean ± SD	Post-HD Mean ± SD	p-value[a] (HD)	Post-AD Mean ± SD	Post-HD Mean ± SD	p-value[a]
14:0	0.324 ± 0.091	0.301 ± 0.068	0.163	0.313 ± 0.068	0.35 ± 0.073	0.001*[e]	0.301 ± 0.068	0.35 ± 0.073	0.001*
15:0	0.161 ± 0.03	0.159 ± 0.026	0.71	0.149 ± 0.049	0.181 ± 0.032	0.001*[e]	0.159 ± 0.026	0.181 ± 0.032	<0.001*
16:0	25.845 ± 1.032	25.705 ± 0.943	0.386	25.768 ± 0.954	26.35 ± 0.721	<0.001*[e]	25.705 ± 0.943	26.35 ± 0.721	<0.001*
16:1n7	0.499 ± 0.189	0.479 ± 0.183	0.492[e]	0.473 ± 0.145	0.547 ± 0.225	0.001*[e]	0.479 ± 0.183	0.547 ± 0.225	0.062
17:0	0.355 ± 0.052	0.361 ± 0.064	0.243[e]	0.354 ± 0.059	0.376 ± 0.07	0.004*[e]	0.361 ± 0.064	0.376 ± 0.07	0.022*[e]
trans-17:1n7	0 ± 0	0.006 ± 0.031	0.992[e]	0 ± 0	0 ± 0	–	0.006 ± 0.031	0 ± 0	0.323[e]
18:0	14.207 ± 1.05	14.053 ± 0.969	0.227	14.063 ± 0.966	14.062 ± 0.91	0.947[e]	14.053 ± 0.969	14.062 ± 0.91	0.842
trans-18:1n9	0.003 ± 0.013	0.005 ± 0.025	0.768[e]	0 ± 0	0.008 ± 0.031	0.162	0.005 ± 0.025	0.008 ± 0.031	0.65[e]
trans-18:1n7	0.062 ± 0.07	0.06 ± 0.086	0.583[e]	0.033 ± 0.059	0.051 ± 0.069	0.115[e]	0.06 ± 0.086	0.051 ± 0.069	0.617[e]
18:1n11	0.048 ± 0.067	0.038 ± 0.069	0.886[e]	0.031 ± 0.055	0.051 ± 0.07	0.078[e]	0.038 ± 0.069	0.051 ± 0.07	0.469[e]
18:1n9	8.755 ± 0.924	8.466 ± 0.872	0.116	8.684 ± 0.859	8.794 ± 0.941	0.335	8.466 ± 0.872	8.794 ± 0.941	0.023*
18:1n7	1.298 ± 0.231	1.322 ± 0.246	0.417[e]	1.336 ± 0.237	1.267 ± 0.201	0.022*[e]	1.322 ± 0.246	1.267 ± 0.201	0.127
18:1n6	0.017 ± 0.06	0.025 ± 0.096	0.36[e]	0.003 ± 0.018	0.01 ± 0.03	0.705[e]	0.025 ± 0.096	0.01 ± 0.03	0.453[e]
18:2n6	17.75 ± 2.679	17.898 ± 2.503	0.667	17.719 ± 2.409	17.234 ± 2.402	0.182	17.898 ± 2.503	17.234 ± 2.402	0.092
20:0	0.546 ± 0.179	0.585 ± 0.151	0.914[e]	0.593 ± 0.149	0.553 ± 0.183	0.035*[e]	0.585 ± 0.151	0.553 ± 0.183	0.184[e]
18:3n6	0.04 ± 0.072	0.031 ± 0.062	0.32[e]	0.037 ± 0.064	0.049 ± 0.077	0.183[e]	0.031 ± 0.062	0.049 ± 0.077	0.088[e]
18:3n3	0.136 ± 0.14	0.121 ± 0.121	0.326[e]	0.125 ± 0.117	0.1 ± 0.119	0.5[e]	0.121 ± 0.121	0.1 ± 0.119	0.334[e]
20:1n9	0.135 ± 0.075	0.14 ± 0.066	0.511[e]	0.145 ± 0.065	0.107 ± 0.067	0.004*[e]	0.14 ± 0.066	0.107 ± 0.067	0.005*[e]
18:4n3	0 ± 0	0.006 ± 0.029	0.973	0 ± 0	0 ± 0	–	0.006 ± 0.029	0 ± 0	0.378
20:2n6	0.295 ± 0.046	0.289 ± 0.051	0.457	0.276 ± 0.094	0.29 ± 0.076	0.57[e]	0.289 ± 0.051	0.29 ± 0.076	0.815
22:0	1.757 ± 0.326	1.78 ± 0.298	0.662	1.769 ± 0.328	1.693 ± 0.286	0.005*	1.78 ± 0.298	1.693 ± 0.286	0.036*
20:3n6	3.757 ± 0.876	3.584 ± 0.811	0.025*	3.616 ± 0.822	3.903 ± 0.862	0.001*	3.584 ± 0.811	3.903 ± 0.862	0.001*
20:4n6	11.65 ± 2.917	11.921 ± 2.724	1[e]	11.804 ± 2.754	11.454 ± 2.313	0.126[e]	11.921 ± 2.724	11.454 ± 2.313	0.034*[e]
20:5n3	1.372 ± 0.545	1.398 ± 0.854	0.782[e]	1.411 ± 0.67	1.543 ± 0.762	0.135[e]	1.398 ± 0.854	1.543 ± 0.762	0.037*[e]
24:0	1.469 ± 0.299	1.482 ± 0.27	0.845	1.472 ± 0.307	1.421 ± 0.266	0.104	1.482 ± 0.27	1.421 ± 0.266	0.047*
24:1n9	2.56 ± 0.442	2.706 ± 0.575	0.009*	2.732 ± 0.493	2.623 ± 0.479	0.019*	2.706 ± 0.575	2.623 ± 0.479	0.27
22:4n6	0.364 ± 0.081	0.357 ± 0.085	0.334	0.354 ± 0.076	0.373 ± 0.082	0.123	0.357 ± 0.085	0.373 ± 0.082	0.117
22:5n6	0.256 ± 0.072	0.255 ± 0.076	0.812	0.244 ± 0.071	0.257 ± 0.063	0.128[e]	0.255 ± 0.076	0.257 ± 0.063	0.873
22:5n3	1.132 ± 0.214	1.083 ± 0.258	0.09	1.098 ± 0.194	1.176 ± 0.208	0.004*	1.083 ± 0.258	1.176 ± 0.208	0.008*
22:6n3	3.603 ± 1.056	3.668 ± 1.059	0.4[e]	3.734 ± 1.047	3.575 ± 1.064	0.056[e]	3.668 ± 1.059	3.575 ± 1.064	0.353[e]
n3/n6 FAs	0.186 ± 0.059	0.187 ± 0.073	0.91[e]	0.19 ± 0.06	0.195 ± 0.068	0.398[e]	0.187 ± 0.073	0.195 ± 0.068	0.217[e]
∑n6 FAs	34.128 ± 2.094	34.361 ± 2.43	0.584[e]	34.053 ± 1.876	33.571 ± 2.293	0.017*	34.361 ± 2.43	33.571 ± 2.293	0.006*[e]
∑n3 FAs	6.244 ± 1.521	6.274 ± 1.866	0.907[e]	6.368 ± 1.64	6.393 ± 1.735	0.916[e]	6.274 ± 1.866	6.393 ± 1.735	0.342[e]
SFAs	44.664 ± 0.927	44.424 ± 0.891	0.113	44.482 ± 0.905	44.987 ± 0.754	<0.001*	44.424 ± 0.891	44.987 ± 0.754	<0.001*
(∑n3 + ∑n6)/ SFAs	0.904 ± 0.042	0.915 ± 0.033	0.213	0.909 ± 0.035	0.888 ± 0.03	<0.001*	0.915 ± 0.033	0.888 ± 0.03	<0.001*
∑cis n3 FAs	6.244 ± 1.521	6.274 ± 1.866	0.907[e]	6.368 ± 1.64	6.393 ± 1.735	0.918[e]	6.274 ± 1.866	6.393 ± 1.735	0.342[e]
∑cis n6 FAs	34.111 ± 2.102	34.336 ± 2.415	0.62[e]	34.05 ± 1.876	33.561 ± 2.294	0.023*[e]	34.336 ± 2.415	33.561 ± 2.294	0.008*
∑trans MUFAs	0.064 ± 0.073	0.07 ± 0.102	0.977[e]	0.033 ± 0.059	0.059 ± 0.077	0.038*[e]	0.07 ± 0.102	0.059 ± 0.077	0.639[e]
∑cis MUFAs	13.316 ± 0.984	13.177 ± 1.197	0.539[e]	13.404 ± 1.02	13.399 ± 1.046	0.989	13.177 ± 1.197	13.399 ± 1.046	0.17
∑cis n6 MUFAs	0.017 ± 0.06	0.025 ± 0.096	0.36[e]	0.003 ± 0.018	0.01 ± 0.03	0.704	0.025 ± 0.096	0.01 ± 0.03	0.453[e]
∑trans FAs	0.064 ± 0.073	0.07 ± 0.102	0.977[e]	0.033 ± 0.059	0.059 ± 0.077	0.038*[e]	0.07 ± 0.102	0.059 ± 0.077	0.639[e]
∑cis FAs	53.671 ± 0.762	53.787 ± 0.82	0.209	53.822 ± 0.848	53.354 ± 0.656	<0.001*	53.787 ± 0.82	53.354 ± 0.656	<0.001*
∑n6 cis FAs	34.128 ± 2.094	34.361 ± 2.43	0.584	34.053 ± 1.876	33.571 ± 2.293	0.017*	34.361 ± 2.43	33.571 ± 2.293	0.006*[e]

[a] p-value based on Mixed model test, fixed effects for pre-post AD and pre-post HD: BMI, Sex, Age, order; fixed effects for post AD-post HD: BMI, Sex, Age, order, order*intervention);[b] p-value based on Mixed model test for FAs with non-normal distribution (normalization: FA +1, probability distribution: Gamma, link function: Log10); fixed effects for pre-post AD and pre-post HD: BMI, Sex, Age, order; fixed effects for post AD-post HD: BMI, Sex, Age, order, order*intervention); *p value < 0.05.

Table 3
Adjusted correlations between phospholipid-derived fatty acids and total dairy intake.

Fatty acids	Coefficient	Confidence interval (95 %)	p value
15:0	0.364	0.218, 0.492	<0.001
17:0	0.321	0.152, 0.482	0.001
18:0	−0.208	−0.355, −0.58	0.036
22:6*n*3	−0.195	−0.345, −0.041	0.049

Partial correlation adjusted for sex, BMI, age, visit number, intervention, and order.

FAs 14:0, 15:0 and 17:0 between the post-AD and post-HD periods, with higher levels after the HD period. Particularly, 17:0 showed a negative correlation with DBP. In contrast, 16:0 and SFAs were positively correlated with both SBP and DBP. Furthermore, machine learning models were applied to predict SBP and DBP.

Results indicated that 14:0, 15:0, and 17:0 levels increased following HD intake compared to AD. Additionally, a positive correlation was observed between 15:0 and 17:0 and dairy intake. Studies have shown that dairy products contribute to total fat and SFAs intake [38]. The 15:0 is found in small amounts in dairy fat, ruminant meat, and fish, while 17:0 is found in ruminant fat. Dairy fat contains approximately 1.0 % pentadecanoic acid and 0.6 % heptadecanoic acid [39]. Research indicates that 15:0 is mainly an exogenous FAs because humans lack the peroxisomal 2-hydroxyacyl-CoA lyase and liver-based α-oxidation

Table 4
Adjusted correlations between phospholipid-derived fatty acids and hemodynamic parameters.

Fatty acids	Coefficient	Confidence interval (95 %)	p value
bSBP			
16:0	0.238	0.149, 0.430	0.035
18:3*n*3	−0.259	−0.391, - 0.082	0.021
SFAs	0.391	0.123, 0.528	<0.001
(∑*n*3 + ∑*n*6)/SFAs	−0.386	−0.499, −0.235	<0.001
∑*cis* FAs	−0.415	−0.491, −0.239	<0.001
bDBP			
16:0	0.327	0.172, 0.442	0.003
17:0	−0.234	−0.434, - 0.147	0.038
18:1*n*7	−0.287	−0.453, −0.111	0.01
20:3*n*6	0.242	0.049, 0.362	0.031
SFAs	0.373	0.210, 0.548	0.001
(∑*n*3 + ∑*n*6)/SFAs	−0.343	−0.559, −0.208	0.002
∑*cis* FAs	−0.381	−0.521, −0.243	0.001
cSBP			
16:0	0.279	0.021, 0.385	0.013
18:3*n*3	−0.272	−0.367, −0.091	0.015
∑*n*6	−0.228	−0.398, −0.036	0.043
SFAs	0.461	0.282, 0.596	<0.001
(∑*n*3 + ∑*n*6)/SFAs	−0.463	−0.574, −0.303	<0.001
∑*n*6 PUFAs	−0.229	−0.423, −0.029	0.042
∑*cis* FAs	−0.495	−0.598, −0.307	<0.001
∑*cis n*6 FAs	−0.228	−0.423, −0.030	0.043
cDBP			
16:0	0.328	0.146, 0.443	0.003
17:0	−0.244	−0.460, −0.141	0.03
18:1*n*7	−0.303	−0.462, −0.138	0.007
20:3*n*6	0.269	0.064, 0.367	0.017
SFAs	0.383	0.246, 0.540	<0.001
(∑*n*3 + ∑*n*6)/SFAs	−0.351	−0.587, −0.212	0.001
∑*cis* FAs	−0.392	−0.533, 0.248	<0.001
cPP			
trans 18:1*n*7	−0.325	−0.456, −0.124	0.003
18:1*n*11	−0.274	−0.442, −0.137	0.014
18:1*n*7	0.278	0.104, 0.518	0.013
18:2*n*6	−0.365	−0.475, −0.074	0.001
18:3*n*6	−0.257	−0.465, −0.001	0.022
18:3*n*3	−0.432	−0.561, −0.270	<0.001
20:3*n*6	−0.279	−0.447, −0.034	0.013
20:4*n*6	0.258	0.074, 0.450	0.022
24:1*n*9	0.319	0.041, 0.473	0.004
22:5*n*3	0.314	0.019, 0.365	0.005
∑*trans* MUFAs	−0.287	−0.454, −0.107	0.01
∑*trans* FAs	−0.287	−0.454, −0.107	0.01
cMAP			
16:0	0.289	0.106, 0.387	0.01
17:0	−0.233	−0.434, −0.131	0.039
18:1*n*7	−0.309	−0.451, −0.111	0.006
SFAs	0.417	0.298, 0.579	<0.001
(∑*n*3 + ∑*n*6)/SFAs	−0.38	−0.591, −0.267	0.001
∑*cis* FAs	−0.434	−0.570, −0.290	<0.001
cAP			
18:3*n*3	−0.29	−0.428, −0.119	0.01
22:0	0.279	0.096, 0.395	0.013
22:5*n*6	0.308	0.085, 0.450	0.006
∑FAs	0.27	0.196, 0.437	0.016
SFAs	0.321	0.091, 0.485	0.004
(∑*n*3 + ∑*n*6)/SFAs	−0.407	−0.509, −0.151	<0.001
∑ *cis* FAs	−0.369	−0.521, −0.128	0.001
cAIx			
22:0	0.282	0.064, 0.375	0.012
22:5*n*6	0.295	0.147, 0.471	0.008
∑FAs	0.24	0.201, 0.410	0.033
SFAs	0.263	0.108, 0.496	0.019
(∑*n*3 + ∑*n*6)/SFAs	−0.343	−0.509, −0.155	0.002
∑*cis* FAs	−0.307	−0.523, −0.135	0.006
cfPWV			
15:0	−0.311	−0.496, −0.130	0.005
18:0	0.308	0.096, 0.505	0.006
18:1*n*7	−0.252	−0.463, −0.032	0.025
22:0	−0.257	−0.440, −0.065	0.022
24:0	−0.292	−0.453, −0.125	0.009
24:1*n*9	−0.242	−0.415, −0.070	0.032
22:4*n*6	0.312	0.130, 0.482	0.005
SFAs	0.278	0.050, 0.487	0.013
∑*cis* FAs	−0.26	−0.471, −0.028	0.021

Partial correlation adjusted for sex, BMI, age, visit number, intervention, order, and dairy intake.

Table 5a
Predictive models for high SBP and DBP using fatty acids data from all four visits.

Features: 16:1*n*7, 20:0, 18:3*n*6c, 18:4*n*3, 22:5*n*3				
Algorithms	Accuracy	Precision	Recall	f1_score
SBP				
Naive Bayes	0.658	0.666	0.971	0.787
KNN	0.660	0.693	0.873	0.771
SVM	0.687	0.703	0.916	0.794
Logistic Regression	0.651	0.689	0.846	0.757
Random Forest	0.642	0.707	0.818	0.749
ANN	0.612	0.711	0.673	0.675
DBP				
Naive Bayes	0.267	0.150	0.111	0.118
KNN	0.815	0.815	1.000	0.898
SVM	0.815	0.815	1.000	0.898
Logistic Regression	0.815	0.815	1.000	0.898
Random Forest	0.805	0.831	0.956	0.889
ANN	0.742	0.818	0.865	0.832

Table 5b
Predictive models for high SBP and DBP using clinical parameters data from all four visits.

Features: waist circumference, HOMAIR, LDL, age				
Algorithms	Accuracy	Precision	Recall	f1_score
SBP				
Naive Bayes	0.695	0.719	0.886	0.790
KNN	0.817	0.843	0.902	0.865
SVM	0.807	0.832	0.900	0.856
Logistic Regression	0.669	0.708	0.845	0.767
Random Forest	0.759	0.780	0.845	0.809
ANN	0.761	0.837	0.830	0.822
DBP				
Naive Bayes	0.787	0.815	0.956	0.879
KNN	0.852	0.880	0.954	0.913
SVM	0.805	0.813	0.989	0.892
Logistic Regression	0.805	0.813	0.989	0.892
Random Forest	0.834	0.876	0.932	0.903
ANN	0.851	0.917	0.907	0.908

Table5c
Predictive models for high SBP and DBP using clinical parameters and fatty acids data from all four visits.

Features: waist circumference, HOMAIR, LDL, age, 16:1n7, 20:0, 20:3*n*6				
Algorithms	Accuracy	Precision	Recall	f1_score
SBP				
Naive Bayes	0.715	0.784	0.789	0.774
KNN	0.762	0.819	0.832	0.817
SVM	0.770	0.790	0.902	0.837
Logistic Regression	0.705	0.738	0.857	0.789
Random Forest	0.760	0.768	0.857	0.830
ANN	0.761	0.821	0.845	0.811
DBP				
Naive Bayes	0.732	0.797	0.899	0.844
KNN	0.872	0.900	0.956	0.925
SVM	0.815	0.815	1.000	0.898
Logistic Regression	0.815	0.828	0.978	0.896
Random Forest	0.853	0.843	0.967	0.905
ANN	0.852	0.912	0.942	0.918

enzymes necessary for its de novo synthesis [40,41]. Limited studies suggest that odd-chain FAs (15:0, 17:0) may be produced de novo via propionate, liver-based α-oxidation, and elongation of 15:0 [40,41]. Therefore, the intake of dietary FAs can have a direct impact on FA composition of circulating lipids and cell membranes [42]. Specifically, 15:0 and 17:0 FAs are commonly used as biomarkers for dairy fat consumption [21]. Studies showing plasma 15:0 and 17:0 levels correlate with total dairy intake [43,44]. In parallel, a meta-analysis demonstrated that plasma/serum levels of 14:0 were correlated with total dairy intake [43]. Although 14:0 has been considered a potential biomarker for dairy consumption, its reliability is lower compared to odd-chain fatty acids such as 15:0 and 17:0. This is because 14:0, while present in dairy products, is also produced endogenously by the human body, limiting its specificity as a marker of dairy fat intake [45]. Overall, this study reconfirms the potential of using 15:0 and 17:0 as reliable biomarkers for dairy intake.

Secondly, 16:0 and SFAs are positively correlated with both SBP and DBP. Similarly, a higher proportion of erythrocytes 16:0 was observed in groups with elevated SBP and DBP [25]. Studies have consistently shown that both free and esterified 16:0 are positively correlated with elevated BP in adults [18,24]. Additionally, studies have indicated that phospholipid and free 16:0 levels are lower in healthy individuals compared to patients with coronary artery diseases [46,47]. The 16:0 is a precursor in ceramide synthesis and contributes to vascular constriction by causing endothelial dysfunction, leading to impaired vessel dilation, increased resistance, and elevated BP. [48]. Overall, the literature supports the link between 16:0 and elevated BP.

Although the current study shows a positive correlation between the sum of SFAs and BP, over 50 % of all SFAs in this study consist of 16:0, which is important to note. A cross-sectional study found that serum total SFAs were higher in individuals with HTN compared to normotensive participants. [18]. Also, a study revealed a positive association between erythrocyte SFAs content and BP; yet, the specific FAs within all SFAs measured was not specified [49].

The current study showed that 17:0 is negatively correlated with DBP and MAP, as well as 15:0 is negatively associated with cfPWV. In patients with diabetes, dyslipidemia, or HTN, 15:0 and 17:0 was found to be inversely associated with arterial stiffness [50]. Elevated amounts of 17:0 have been correlated with reduced levels of total cholesterol, triglycerides, apolipoprotein A-1, apolipoprotein B, and hepatic markers [51]. However, a study has found no association between 17:0 and BP [52]. Overall, the relationship between dairy product intake and BP may be multifaceted [29]. Even if 16:0 intake may negatively impact cardiovascular health, other nutrients in dairy products, such as odd-chain FAs, protein, potassium, and magnesium, could contribute to beneficial effects on blood pressure and arterial stiffness [29,53,54].

HTN is influenced by a combination of modifiable and non-modifiable risk factors [55]. Addressing modifiable risk factors through lifestyle changes can reduce the risk of developing HTN [56]. In this study, machine learning techniques were utilized to develop predictive models for HTN. For SBP prediction using clinical parameters, KNN algorithm achieved the highest performance, with an accuracy of 0.817, demonstrating its effectiveness in identifying individuals with elevated SBP. For DBP prediction, incorporating FAs data alongside clinical parameters further enhanced the model's performance. The KNN model emerged as the top performer, improving its accuracy to 0.872, highlighting the added value of FAs in refining the predictive capability for DBP classification. First, as the mean age of the population increases, the prevalence of HTN rises [57]. Secondly, a strong association between waist circumference and HTN has been demonstrated. Larger waist circumferences have been linked to an increased risk of HTN due to its reflection of visceral fat [58–61]. Thirdly, previously a study found a relationship between HOMA-IR and SBP and DBP, indicating that higher insulin resistance is associated with increased BP [62]. Another study confirmed the association of higher HOMA-IR levels with primary HTN, independent of other factors like obesity and diabetes [63]. Forth, a Mendelian randomization analysis demonstrated that the risk of HTN increased in both men and women as LDL levels increased [64]. Fifth, a study demonstrated that individuals with pregnancy-induced HTN had lower levels of VLSFAs, with 20 carbons or more, such as 20:0, as well as a decrease in the sum of VLSFAs, compared to the control group [65]. Moreover, elevated circulating levels of VLSFAs have been correlated with a reduced risk of T2D, atrial fibrillation, and coronary disease [66]. Finally, studies have shown that patients undergoing coronary angiography and those with coronary artery disease have higher levels of 20:3*n*6 compared to healthy individuals [46,47]. 20:3*n*6 has also been positively correlated with BP in adults and SBP in children [18,24,67]. However, two studies found no correlation between 20:3*n*6 and BP [52,68]. 16:1*n*7, while a MUFA, may behave more like an even-chain SFA by increasing insulin resistance, heart rate, and influencing total and LDL cholesterol levels [69]. A study found that 16:1*n*7 raises LDL cholesterol more than 16:0, potentially affecting BP [69]. Two observational studies in adults and additional studies in obese children reported a positive association between 16:1n7 and BP [24,25,67,70]. Conversely, a study found a negative correlation between 16:1*n*7 and diastolic BP in adults at high risk of CVD [52], while another found no correlation with erythrocyte membrane 16:1n7 and BP [68]. These findings suggest a complex and mixed relationship between 16:1*n*7 and BP, indicating the need for further research. Overall, this study demonstrates that machine learning models can predict HTN by identifying and incorporating risk factors [23–25]. The study highlights the potential of integrating clinical parameters and circulating fatty acids into predictive models for hypertension risk. These models could enable early identification of at-risk individuals, providing opportunities for personalized dietary interventions and better hypertension prevention strategies in clinical practice [71,72].

This study has several strengths and limitations. Advanced statistical methods (GLMM) and machine learning models were used, enhancing analytical precision and innovation. The crossover design reduced intergroup variability, and the flexibility in dairy product selection reflected real-life intake patterns, with higher serum levels of 15:0 and 17:0 indicating good compliance during the HD phase. This study's highly selected population may introduce selection bias, limiting model generalizability. While performance was strong within this group, validation in larger, more diverse cohorts is needed for broader clinical applicability. The six-week intervention might not capture long-term effects, and the lack of a control group without dairy intake prevents assessment of dose-response effects on vascular function. According to Health Canada and dietary guidelines, dairy products contribute essential nutrients such as calcium, vitamin D, and protein, yet many Canadian adults do not consume enough dairy to meet recommended intakes. The 2007 Canada's Food Guide suggested two servings of dairy per day for adults aged 19–50 and three servings per day for those aged 51 and older [73]. The Dietary Approaches to Stop Hypertension (DASH) diet recommends consuming 2 to 3 servings of low-fat or fat-free dairy products daily to help lower blood pressure and improve heart health [74]. However, the 2015 Canadian Community Health Survey (CCHS) reported that the average dairy intake among adults was approximately 1.36 servings per day [73]. Similarly, data from the National Health and Nutrition Examination Survey (NHANES) 2013–2014 indicate that American adults aged 19–50 years consume approximately 1.7 servings of dairy per day [75], which remains below the recommended levels.

5. Conclusion

The findings underscore the potential of using specific FAs as biomarkers for dairy intake and predictors of HTN risk. Additionally, the integration of machine learning techniques demonstrated highly predictive accuracy for HTN, suggesting the value of combining clinical parameters and FA profiles in risk assessment. The results of this study contribute to a better understanding of the complex relationships

between dietary fats, and BP, highlighting the importance of distinguishing between different FAs when considering their health impacts.

Author contributions

H Arghavani: Conceptualization, Formal analysis, Writing - Original Draft, Writing - Review & Editing, Visualization. JF Bilodeau: Supervision, Writing - Review & Editing, Resources. I Rudkowska: Conceptualization, Supervision, Writing - Review & Editing, Resources.

Availability of data

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Declaration of competing interest

All authors state that there is no conflict of interest.

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