Biomarkers and Lifestyle Risk Factors for Hypertension in Elderly Australians

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Abstract

Hypertension is an easily tested and treated risk factor of cardiovascular disease, stroke, atherosclerosis, and Type 2 Diabetes. A thorough understanding of lifestyle and nutrition factors affecting hypertension is essential for reducing the prevalence of hypertension in patients of all ages, as well as designing treatment and prevention procedures for other diseases. Lay audience understanding and knowledge is lacking around simple ways to reduce hypertension risk. To gain a broad picture of such factors, machine learning methods, including random forest, logistic regression and classification trees, were undertaken on Australian Health Survey 2019 data from the Australian Bureau of Statistics. Variable importance and their impacts on hypertension were identified, then confirmed by hypothesis testing of means on nutrient intake for hypertensive and non-hypertensive groups. Several factors were identified as predictors of hypertension in elderly (>60) Australians including BMI, waist circumference, caffeine, alcohol consumption, trans-fatty acid consumption, cholesterol consumption, and diabetes status. Many of these risk factors can be reduced with simple education around physical activity, weight loss, and dietary changes, making this research ideal for addressing the Australian population to reduce the prevalence of hypertension and its follow-on diseases.

Introduction

More than 4.1 million Australians have uncontrolled hypertension (1). Despite over $2 billion AUD spent annually on prevention, hypertension is still found in 35% of all people over 18. Over 40% of Australians between 65 and 85 have hypertension, which is over a third of the population over 65 (2). Left unchecked, hypertension is a precursor to complications of greater burden such as heart attacks, aneurysms, metabolic syndrome, and dementia. Determining the lifestyle factors which are contributors to hypertension is of the utmost importance to reduce the prevalence of hypertension and its follow-on diseases (3). Given the ageing population of Australia and age also being a significant risk factor for hypertension, studies finding ways to prevent hypertension are crucial (4).

The symptoms of hypertension can be easily overlooked or not observed, as hypertension can only be detected when individuals have their blood pressure checked manually (1). The risk factors giving rise to hypertension are increasingly becoming the norm today. These risk factors include poor diet, being overweight or obese, insufficient physical activity, excessive alcohol consumption, and smoking. However, the specific dietary patterns of individuals, particularly the elderly, with hypertension are not completely understood. It is widely known that high sodium is a large contributor to hypertension, but other biomarkers, such as fat, cholesterol, and lean meat consumption, have also been linked to hypertension (2,5).

Hypertension refers to a measured blood pressure higher than 120/80 mmHg, which is the considered the value of the limit of the normal blood pressure range. Any value above this is considered hypertension, with varying degrees of severity above that. The first number refers to systolic blood pressure (SBP), recorded as blood is pushed away from the heart, where the second number is diastolic blood pressure (DBP), recorded as the heart fills with blood (6). Uncontrolled hypertension refers to hypertension that is not controlled by medication. In Australia, men are 25% more likely to have uncontrolled hypertension than women (2). SBP has been shown to rise with advancing age, explaining the increasing prevalence of hypertension as individuals become older. On the other hand, DBP plateaus at the age of 50 and declines thereafter (7).

The Renin-Angiotensin II-Aldosterone system (RAAS) is critical to blood pressure regulation. Normally, renin is released and converts angiotensin I into angiotensin II in response to lowered blood volume from water and/or salt secretion. Aldosterone and ADH are secreted in response to angiotensin II to increase salt and water retention, respectively, increasing blood volume and subsequently blood pressure. In hypertensive patients, the RAAS system can be activated as a result of renal artery stenosis. The system recognises a loss of blood volume in the kidneys and thus activates RAAS in order to increase blood volume. This chronically increases blood volume and thus blood pressure in hypertensive patients (8-9).

Currently, the most effective approach to curing and preventing hypertension without medication is a dietary one, especially the DASH diet. This approach emphasises limiting sodium, saturated fat and sugar intake, as well as increasing intake of protein, fibre, potassium, magnesium and calcium (10). There is abundant existing evidence to suggest that hypertension can be controlled without medication, with a healthy diet having a long-term positive influence on hypertension and cardiovascular risk (11).

The present study extended insight into previous literature on investigating the prevalence of hypertension in individuals who do and do not engage with these identified risk factors. Utilising data science and investigating data collected over two observation periods, the effect of biomarkers, lifestyle, and nutrition factors on hypertension was observed. These factors were analysed through machine learning algorithms along with literature review to make qualitative observations linked to hypertension. Waist circumference, BMI, age, cholesterol level, diabetes status, and smoking status had different magnitudes of effect between sexes. Consumption of fruit and vegetables, fatty acids, alcohol, and caffeine were all good predictors of hypertension in individuals over 60 years of age. These analyses found good predictors of hypertension, which combined, are a set of preventable risk factors.

Results

In the following research we have defined elderly as older than 60.

Male Biomarkers and Lifestyle Factors

Initial plotting of the elderly male dataset was carried out to observe any patterns, however a T-SNE plot with the optimal number of 2 clusters did not display any significant patterns, (Fig. 1). After assessing model performance, Random Forest was found to be the best performing model (Fig. S14-16). Visualising variable importance based on the decrease of mean Gini scores indicates that body mass index (BMI) score and measured waist circumference (WC cm) had the two highest decrease in Gini score (Fig. 2). Following these is age, number of daily serves of vegetables, cholesterol levels, and number of daily serve of fruits. Smoking, diabetes status, and high sugar levels have significantly lower mean decrease in Gini score. Additionally, adherence to dietary guidelines is the least influential, which could be due to 94% of the participants not following the recommended dietary guidelines (Fig S3).

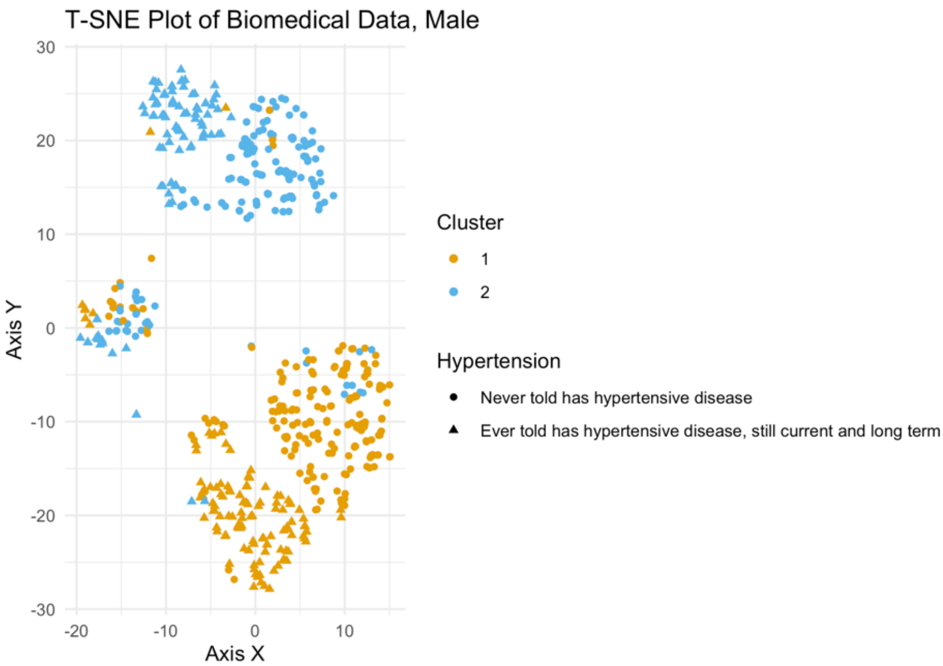

Figure 1. T-SNE Plot of Biomedical Data, male. T-SNE plot is a dimensional reduction method where similar objects are modelled by nearby points. It consists of three steps; (1) Constructing a probability distribution over parts of high-dimensional objects; (2) Defining similar probability distribution over the points; (3) Minimising Kullback-Liebler divergence between two distribution. Although there are three groups of points, labels show to a particular pattern.

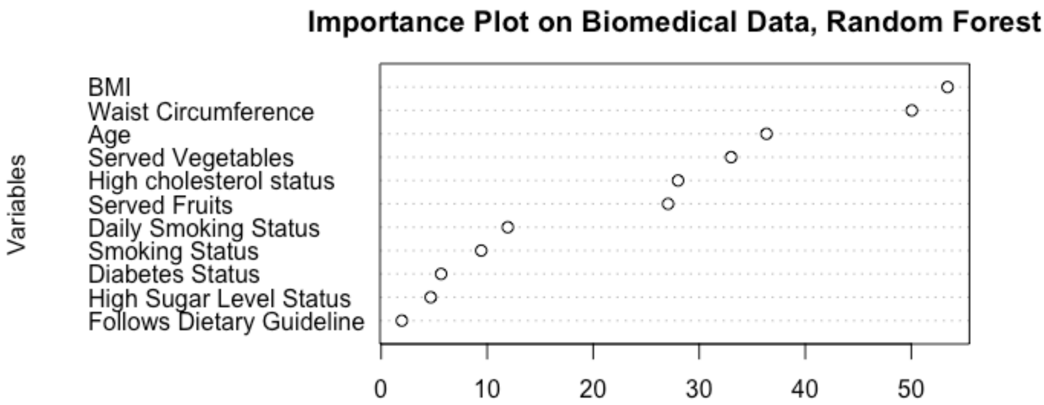

Figure 2. Importance (Mean decrease of Gini). Gini Index is the probability of a feature that is classified incorrectly when randomly selected. This plot shows the mean decrease of Gini Index featuring the variables. BMI, WC, served vegetables, cholesterol status, and served fruits have high mean decrease of Gini, meaning the chance of them classifying incorrectly is smaller.

For numerical factors (age, BMI, WC), the partial dependence plot shows that with decreasing contribution to no hypertension, the value increases (Fig. S2). For the more important categorical variables, having high cholesterol contributes more to hypertension while eating less than 1 serve or eating 5 or more serves of vegetables daily has a smaller relative logit contribution compared to other categories (Fig. 3).

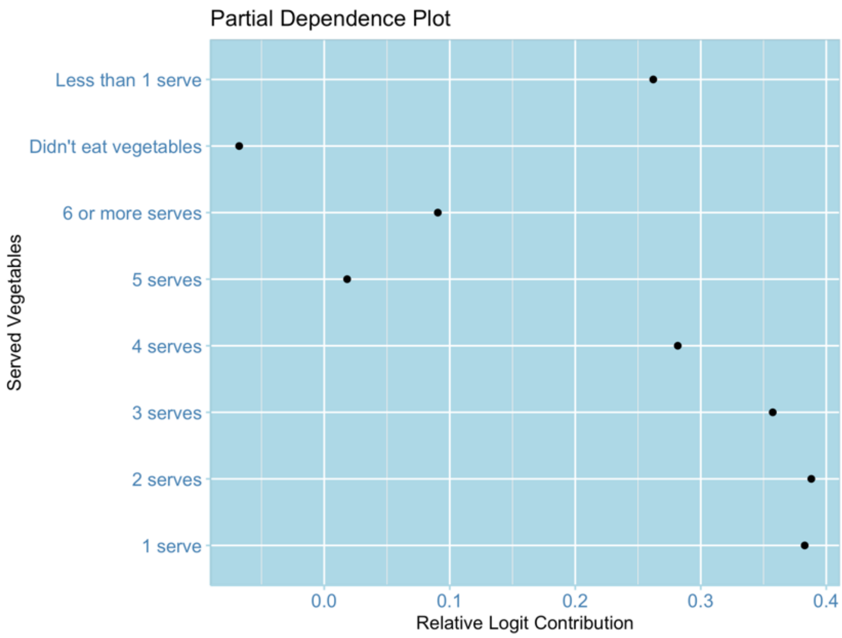

Figure 3. Partial Dependence Plot of Number of Served Vegetables. The plot displays the relative contribution of the value to no hypertension. Hence, eating five serves or more, or less than one serve contributes less to a healthy lifestyle. Meanwhile, eating a moderate amount of vegetables helps in preventing hypertension.

Plotting the less important variables by the two groups also explains why they have less impact on hypertension; the proportion of high sugar levels, people with diabetes, and smokers are similar in both groups (Fig. S3-5). Although the variable importance plot suggests the number of daily serves of fruits is important, there were no unique patterns during visualisation of the variable and the partial dependence plot suggested no pattern (Fig. S11).

On the contrary, a large proportion of individuals currently without hypertension were never told of having high cholesterol (Fig. S6-7). Additionally, many individuals with low or high vegetable intake have hypertension (Fig. S8). The boxplots of age, BMI, and WC displayed some differences between the two groups (Fig. S10). Wilcoxon sum-rank tests were conducted on these variables with null hypothesis of equal means between groups. The mean for the alternative hypothesis of the hypertensive group was greater, equalling 0.05. In all three cases, the null hypotheses were rejected (Table S1).

Overall, the best performing model, Random Forest, selected BMI, WC, age, number of daily serves of vegetable and fruits, and high cholesterol status as the most significant in predicting hypertension.

Male Nutrition Factors

In the nutrition dataset, ridge logistic regression performed the best (Fig S17-19). Looking at the coefficient of the variables in the model, polyunsaturated fat had a negative coefficient (Fig. 4). The rest of the nutrients had positive coefficients with the largest being percentage energy intake from trans fatty acid and alcohol consumption (grams and percentage of energy). The amount of water, sodium, and trans fatty acid (g) consumed had almost insignificant coefficients in the logistic regression model.

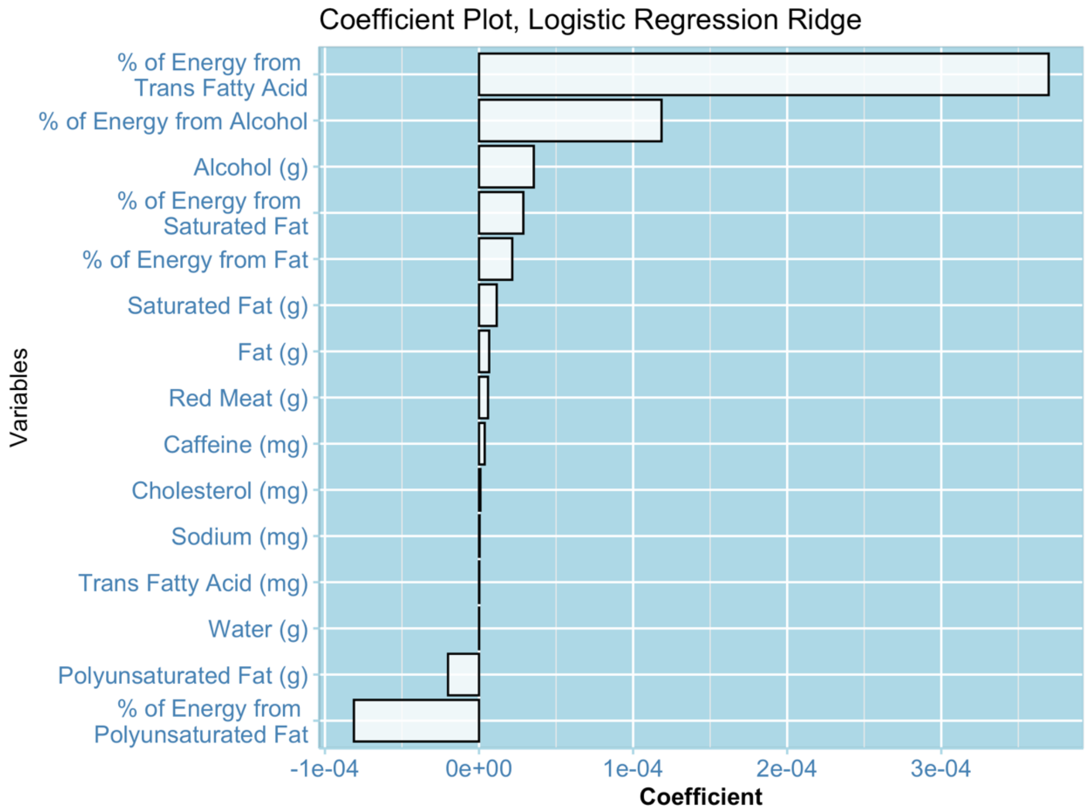

Figure 4. Coefficient of Logistic Regression, Male. The coefficients show the scale in which the variables impact hypertension in terms of one-unit increases. Therefore, alcohol (g) and trans fatty acids (%) have a higher impact on male hypertension, while polyunsaturated fat could contribute to a healthier lifestyle due to its negative coefficient.

The boxplots of the nutrients showed almost no differences between the two groups, due to similarly sized boxplots with similar median values in each nutrition variable (Fig S12-13, S22-23). Many participants did not consume red meat on the interview day and the only significant difference was in alcohol consumption between the two groups. Individuals with hypertension had higher median values of alcohol consumption and a wider third quantile. Excluding alcohol, caffeine, and red meat consumption, none of the Wilcoxon sum-rank test rejected the null hypothesis (Table S1). The alternative hypothesis was accepted for people with hypertension who also had a higher mean score for alcohol, caffeine, and red meat consumption.

Overall, besides polyunsaturated fats, all nutrients could contribute to hypertension, with percentage of energy from trans-fatty acid and alcohol consumption having the highest contribution in terms of unit increase.

Female Biomarkers and Lifestyle Factors

The investigation into the significance of biomarkers and lifestyle factors in hypertension was continued in elderly females. The biomedical data consisted of 733 individuals, 274 still currently with hypertension either long or short term, and 459 individuals who had recovered or never been diagnosed. The performance of classifiers can be compared to the one-rule classification algorithm as a baseline, which labels all instances of the focus variable as the most common instance in that variable. Here, the one-rule algorithm classified all individuals who had never or no longer had hypertension as the most common at 459 of 733. This algorithm has an accuracy percentage of 62.62%.

The forward and backward stepwise selection on the LDA model produced two different models. The forward stepwise concluded with BMI as its only predictor variable, while the backward stepwise included WC and measured weight. Both the forward and backward stepwise models for the QDA converged, with only WC as their predictor variable. Overall, using a cross validation repeated 200 times, these models were only slightly better than the one-rule algorithm with average accuracy performances of 63.39% and 63.38% for the forward and backward stepwise LDA respectively, while the QDA model had an average accuracy of 63.55% (Fig. 5).

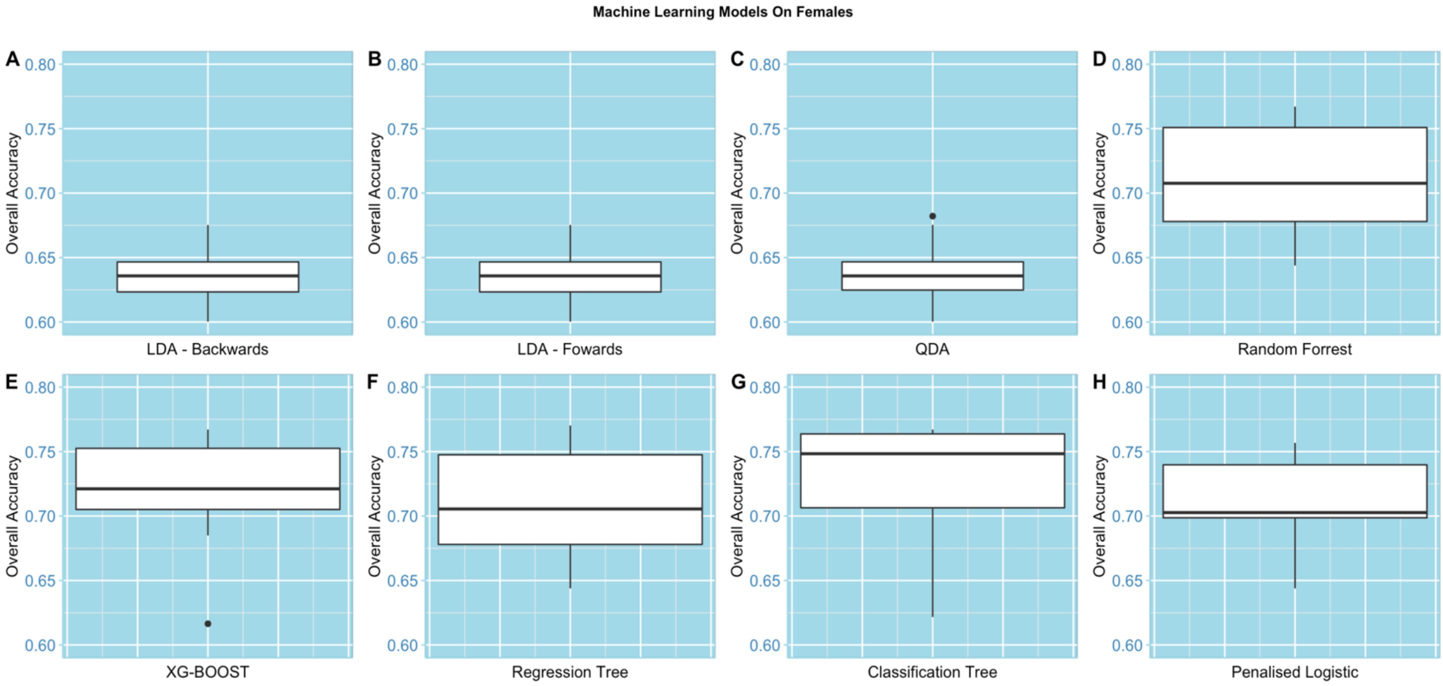

Figure 5. Performance of Classifiers. (A-H) The boxplots reflect the performance of each classifier at predicting hypertension. (A-C) These are models that used only numerical portion sof the dataset. (D-H) Models that were built on the entire data frame. A-C are models that were built using the Ida and Qda functions inside the MASS package. D-H were build using train inside the Caret package. The performance of all classifiers is on the same axis and are directly comparable to each other. D, E-H represent the highest performing algorithms, however, H provides equivalent performance whilst having a visually lower variance.

The classification and gradient boosting tree algorithms and the elastic net logistic regression outperformed all the other models. Of these, the gradient boosted tree algorithm and elastic net logistic models were very close in prediction accuracy with accuracy means of 72.42% and 72.45%, respectively (Fig. 5). However, when considering the distribution of accuracy, the gradient boosted trees had a higher variance, which implies inconsistent results. As such, the elastic net was selected as the best performing model for this dataset.

The most important variables identified were cholesterol and whether individuals met the recommended dietary guidelines for fruits and vegetables. The subsequent most important variables were diabetes status, high sugar in blood/urine, age, smoker status, serves of fruit, WC, and BMI. The logistic regression results showed that increases in cholesterol, blood/urine scores, smoking status of individuals, and being classified as having diabetes increased the likelihood of an individual being classified with hypertension. Satisfying the daily recommended daily intake showed the highest influence in decreasing the likelihood of being classified with hypertension, while increasing age, fruit consumption, waist circumference, and BMI showed lower influence (Fig. 6).

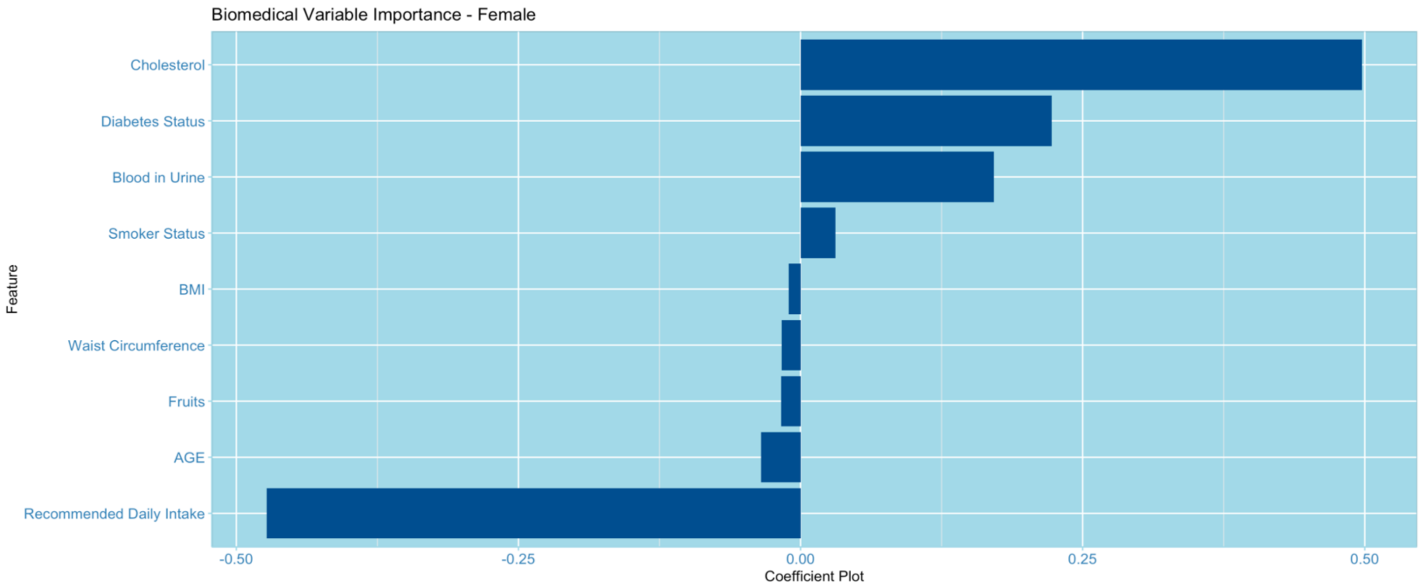

Figure 6. The coefficient of variables and their weightings as contributors to hypertension. The magnitude of the direction from 0 on either side reflects importance; larger magnitude indicates greater importance. Direction indicates whether the factor increases or decreases the likelihood of a hypertension classification. The plot comes from a trained logistic regression model using the train function within the Caret package. Using a 10-fold cross validation, the model with the highest accuracy is selected. Cholesterol, diabetes, blood in urine, and smoker status increase hypertension likelihood. Satisfying recommended daily intake reduces this risk. Increases in BMI, WC, fruit consumption, and age increase likelihood.

Female Nutrition Factors

The same methods as above were applied to the nutrition data set, with the classification tree having the highest performance based on accuracy. Percentage of energy from alcohol and trans fatty acids were removed due to their high collinearity with the remaining variables. For the classification tree, the variables were similar in their importance, with cholesterol being the most important feature of the model. Polyunsaturated fats and percentage total energy from fats showed lower but similar levels of importance. Percentage energy from trans fatty acids, saturated fats, sodium, percentage of energy from unsaturated fats, caffeine, red meat consumption, and alcohol were the next most important variables considered (Fig. 7).

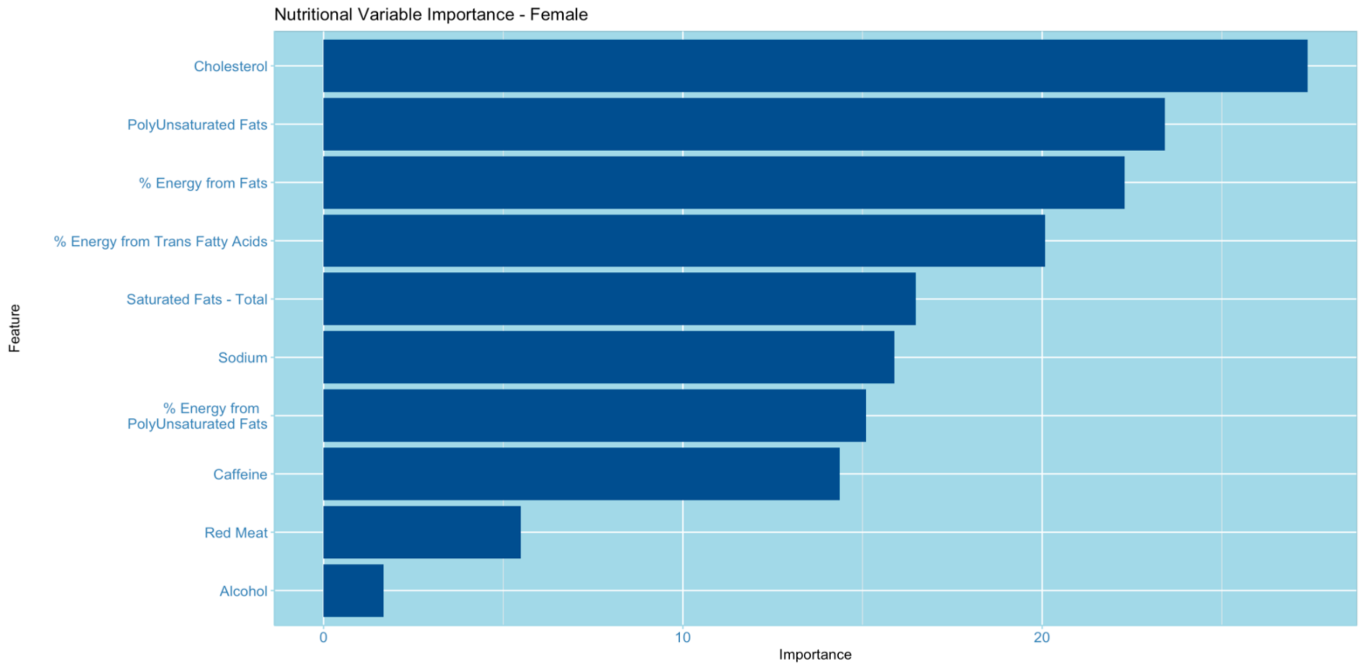

Figure 7. Variable Importance within the classification tree for nutrition data. Larger magnitude indicates greater importance. The variable importance here is relative and importance is not indicative of predicative capabilities. Variable importance is an attribute of a trained r-part object. The model was created using the train function inside the Caret package with a 10-fold cross validation. Most variables are relatively important except for red meat and alcohol. This importance graph does not show directionality.

From an examination of the partial dependence plots (Fig. S9, S20-21), increases in cholesterol, and percentage of energy intake from fats were the largest contributors in increasing an individual's likelihood being classified with hypertension. Alcohol and caffeine did so with lesser importance. An increased intake of polyunsaturated and saturated fats were the most important features in reducing this likelihood, as well as the consumption of trans fatty acids and sodium.

Comparing Sexes

Comparing the nutrition intake of both sexes with boxplots, the median values of boxplots for males were equal or higher than those of females (Fig S12-13, S22-23). The boxplots suggested low alcohol and meat consumption for both sexes, but the third quantile of the boxplots was larger for men than for women (Fig S12). Male Boxplots for almost all nutrition factors were at least as spread as the boxplots for female. Boxplots of men with hypertension had higher third quantile and/or higher median values, inconsistent with females. Conducting a Chi-Square test of independence also suggested no dependency of hypertension on sex.

Discussion

The major causes of mortality in elderly individuals in Australia are cardiovascular disease (CVD), coronary heart disease (CHD) and stroke. Hypertension is a major risk factor for these diseases (7), along with atherosclerosis and Type 2 Diabetes (T2D). Having a BMI above 30 also increases hypertension risk due to age-related metabolic alterations (12). Moreover, hypertension is known to worsen complications of diabetes through diabetic nephropathy or retinopathy (13). High consumption of cholesterol, trans-fatty acids, high fat foods, caffeine, alcohol, and smoking have been associated with hypertension (7, 14-16).

Biomedical Data

Overweight and obese BMIs have a significant relationship with hypertension. Our results showed BMI as one of the strongest risk factors for hypertension, more so in males than females. Results from both sexes illustrated that an above healthy BMI increased prevalence of hypertension.

Waist circumference (WC) was also strongly associated with hypertension in elderly individuals, more accurately than BMI as it accounted for body fat distribution (17). WC over 102cm and 88cm for men and women respectively, is considered high risk for obesity, dyslipidemia, and visceral adiposity, which are constituting factors for hypertension (17). Our results indicated WC was a greater risk factor for males than females.

Our analyses demonstrated that prevalence of hypertension increased with advancing age. This is consistent with Australian Institute of Health and Welfare (AIHW) data, stating that hypertension prevalence peaks at 47% in people over 85 (2). The main mechanism for BP control is the RAAS system, which atrophies with increasing age. Reduced RAAS activity may lead to decreased responsiveness to angiotensin blockers. The difference between DBP and SBP usually increases with age due to progressive central arterial stiffening. These factors lead to increased risk of chronic hypertension (18).

Daily fruit and vegetable servings had a moderate effect on the prevalence of hypertension in both sexes, with vegetable serves showing reduction in hypertension risk for men and women. Previous meta-analyses detail an inverse association between fruit and vegetable consumption and hypertensive risk (19). While the mechanisms are currently unknown, speculation pertains around the flavonoid content of some fruits and vegetables, including anthocyanin and quercetin. Quercetin has an antihypertensive effect through its ability to regulate the RAAS system and vascular smooth muscle contractility, inducing vasodilation (20).

Diabetes was found to increase the risk of hypertension in women. In diabetes, high sugar was observed in urine which predisposes arteries to atherosclerosis. This was not observed in men, however this finding was unsupported in literature and requires further investigation (13).

Nutrition Data

High percentage fat intake was associated with hypertension factors. Literature indicates links with CVD complications. The differences between male and female fat intake in relation to hypertension is currently inexplicable. It is hypothesised that a larger dataset would not present this discrepancy.

Trans-fatty acids were a predictor of hypertension in both sexes. No recent studies have shown a relationship between high trans-fatty acid intake and hypertension (15-16), but the correlation is likely linked to negative effects of trans-fatty acids in atherosclerosis. Analysis showed that high mono and polyunsaturated fatty acid intake decreased hypertensive risk in both sexes. Mono- and polyunsaturated fat intake has been associated with lower blood pressure; however, the mechanisms are largely unknown (21-22). It was unclear why these results differed in men and women. Again, this may be due to a small dataset.

This study demonstrated high cholesterol levels in both sexes as a predictor of hypertension. The mechanism of this contribution was unclear, however, increasing low-density lipoprotein (LDL)-cholesterol without increasing high-density lipoprotein (HDL)-cholesterol destabilises the LDL:HDL ratio, predisposing the body to CVD (23). which could explain the observed correlation (18).

Alcohol consumption was associated with hypertensive risk; however, this differed between sexes (24). The data demonstrated an increasing risk of hypertension in elderly males, but less impact on females. SBP in heavy drinkers was increased by 5-10mmHg. Alcohol causes the autonomic nervous system to acutely raise blood pressure (25). The difference between sexes is possibly due to alcohol metabolism, drinking times, and patterns. Although irregular heavy drinking impacted blood pressure, the extent of alcohol consumption causing hypertension is unclear due to insufficient cohort studies investigating these effects (24).

Caffeine has been associated with high blood pressure. Caffeine continuously opens intracellular calcium stores of myocardium, increasing heart muscle contraction and subsequently cardiac output (26-28). There are no counteractors to the open state of sarcoplasmic reticulum after caffeine consumption, therefore caffeine acutely raises blood pressure 30-60 minutes post-consumption. Studies have failed to concede whether caffeine chronically increases blood pressure (29). Our analyses suggest that increased hypertensive risk is associated with increased caffeine consumption, presenting a potential risk factor for the elderly population.

Smoking was also a predictor of hypertension. Studies have shown smoking as a risk factor, strongly associated with oxidative stress which alters mitochondrial functioning, contributing to endothelial dysfunction (20, 30). The differences in impact between the sexes is unknown (7).

Studies have emphasised hormonal differences, gene variability, and other gender differences, as large contributors to differences in epidemiology, pathophysiology, and treatment of hypertension between men and women. Estrogen has an impact on the vascular system, through vasodilatation, inhibiting vascular remodelling processes, and modulating the RAAS and sympathetic system. During reproductive age, this induces a protective effect on arterial stiffness, but reverses after menopause (31).

Treatment and prevention of hypertension can occur through weight loss and simple dietary changes. Weight loss medications, like Sibutramine, dramatically reduce blood pressure in the elderly (32).

Lowering dietary cholesterol intake is also a primary recommendation for individuals with hypertension (33), alongside reducing dietary fat (7). Further studies and meta-analyses with more data are required to confirm the effects of all identified risk factors in the current study.

Limitations

During the cleaning process, many important variables that may have provided insight, such as cholesterol level, were removed due to large amounts of missing data. The dataset was only made up of 1321 participants whereas Australia recorded 515,700 people aged 85 or above in 2019 (34). This limitation prevented a confident result. Collecting more complete samples with more health factors is necessary for more reliable conclusions to be made. Other limitations included computer hardware. Machine learning models required fast and modern GPUs or CPUs for complex models like Random Forest, a model built up from multiple classification models. It was computationally expensive to train multiple models and compare them with one another. One possible remedy could be cloud computing or gaining access to a more powerful machine.

Methods

Data was retrieved from the Australian Health Survey conducted by the Australian Bureau of Statistics (ABS) in 2019 (34) to obtain national benchmark information on health-related issues. The survey was designed to ensure that within every state and territory, each person could be selected from any age from a non-remote area of Australia and that reliable results could be produced for each state and territory. Face-to-face interviews were conducted by trained ABS interviewers, asking candidates about their health condition, lifestyle, eating patterns, and other health risk factors, such as social, economic, and environmental factors.

A subset of this data was provided by The University of Sydney in four different files including metadata that was partially cleaned. This included a dataset with biomarkers and lifestyle factors of individuals, a nutrition dataset that described the nutritional intake of participants for two days, and a food dataset that detailed food consumption of participants on eating occasions for two days. This data was used for analytics combined with literature review to answer our research questions.

Before analysis, the dataset was partially cleaned, with empty rows, columns, constant variables, and duplicate rows removed and variables transformed into correct types. To account for missing values, combinations of rows and columns were deleted with intention of keeping as many samples as possible. Columns were created with Boolean values to denote outliers in numerical variables. The dataset was then reduced to keep Australian people over 60 only and separated by sex. Finally, the variables that explained hypertension were modified and two groups were created: people with hypertension currently, and people without hypertension currently, including those previously diagnosed but now recovered. Consultation with nutrition and physiology experts allowed us to select relevant variables for analysis (Table 1).

Table 1. The biomarkers, lifestyle factors, and nutrition selected for association with hypertension with 588 elderly males and 733 females.

Biomarkers	Lifestyle Factors	Nutrition
• BMI • Age • Measured Waist • Diabetes Status • High Cholesterol Status • High Sugar Level Status • Hypertension	• Number of daily serves of fruit and vegetables • Smoking Status • Daily smoking status	• Red Meat • Alcohol • Different Fats • Caffeine • Water Consumption • Cholesterol Consumption • Sodium Consumption

Data Analysis

The first step was to visualise the biomedical data to find any unusual patterns. A T-SNE plot was generated with Gower distance, allowing for visualisation of a high dimensional dataset with categorical and numerical variables. For the nutrition data, a PCA plot was generated as all values were numerical. To further isolate variables that could contribute to hypertension and understand their impacts, various supervised machine learning techniques were applied to the biomedical dataset, including:

- Classification Trees
- Logistic Regression (BIC, AIC, LASSO, and Ridge)
- Linear and Quadratic Discriminant Analysis
- Random Forest

For discriminant analysis and logistic regression models, stepwise variable selection was applied, where the starting models were the full model and the model with no predictor variable. Five-cross-fold validation was used with F1-score or overall accuracy to assess the performance of the classification algorithms on samples created from the original cleaned dataset with replacement. For each cross-fold validation, four folds were used as training sets to build the models, with one used to test the performance. This method was repeated 200 times and the results were plotted with boxplots. The best performing model was selected to plot the importance and effects of variables. For numerical variables, after removing the outliers, hypothesis testing was conducted on the mean values to compare the groups of people with hypertension and without hypertension. Variables were also visualised by hypertension group to understand the order of importance. The results obtained along with a literature review made it possible to link food intake to hypertension and observe dietary differences between individuals with and without hypertension using the food and nutrition datasets. These were all carried out using R language.

A literature review was undertaken to investigate existing information about hypertension in people aged over 60. Hypertension was researched in conjunction with the following factors: cholesterol, diet, fruit, vegetables, meat, obesity, diabetes, smoking, caffeine, and alcohol consumption. This helped in expanding knowledge of potential nutritional factors for developing hypertension and guided the selection of variables for statistical analysis. Literature sources used included the University of Sydney Library, PubMed, other online databases, and reputable websites like the World Health Organisation and the Australian Institute for Health and Welfare (AIHW). The AIHW also provided recent statistical information regarding hypertension in Australia.

Author Contributions

Conceptualisation, 480398736, 480383765, 480556196, 480133780, 480194817, 480427047; Validation, 480556196, 480133780; Formal Analysis, 480556196, 480133780; Investigation, 480398736, 480383765, 480194817, 480427047; Resources, 480398736, 480383765, 480194817, 480427047; Data Curation, 480556196, 480133780; Writing – Original Draft, 480398736, 480383765, 480556196, 480133780, 480194817, 480427047; Writing – Review and Editing, 480398736, 480383765, 480194817, 480427047; Visualisation, 480398736, 480383765, 480194817, 480427047; Project Administration, 480133780, 480194817, 480427047.

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