Protein for hypertension: the whey to go?

Whey protein lowers blood pressure and improves endothelial function and lipid biomarkers in adults with prehypertension and mild hypertension: results from the chronic Whey2Go randomized controlled trial

Introduction

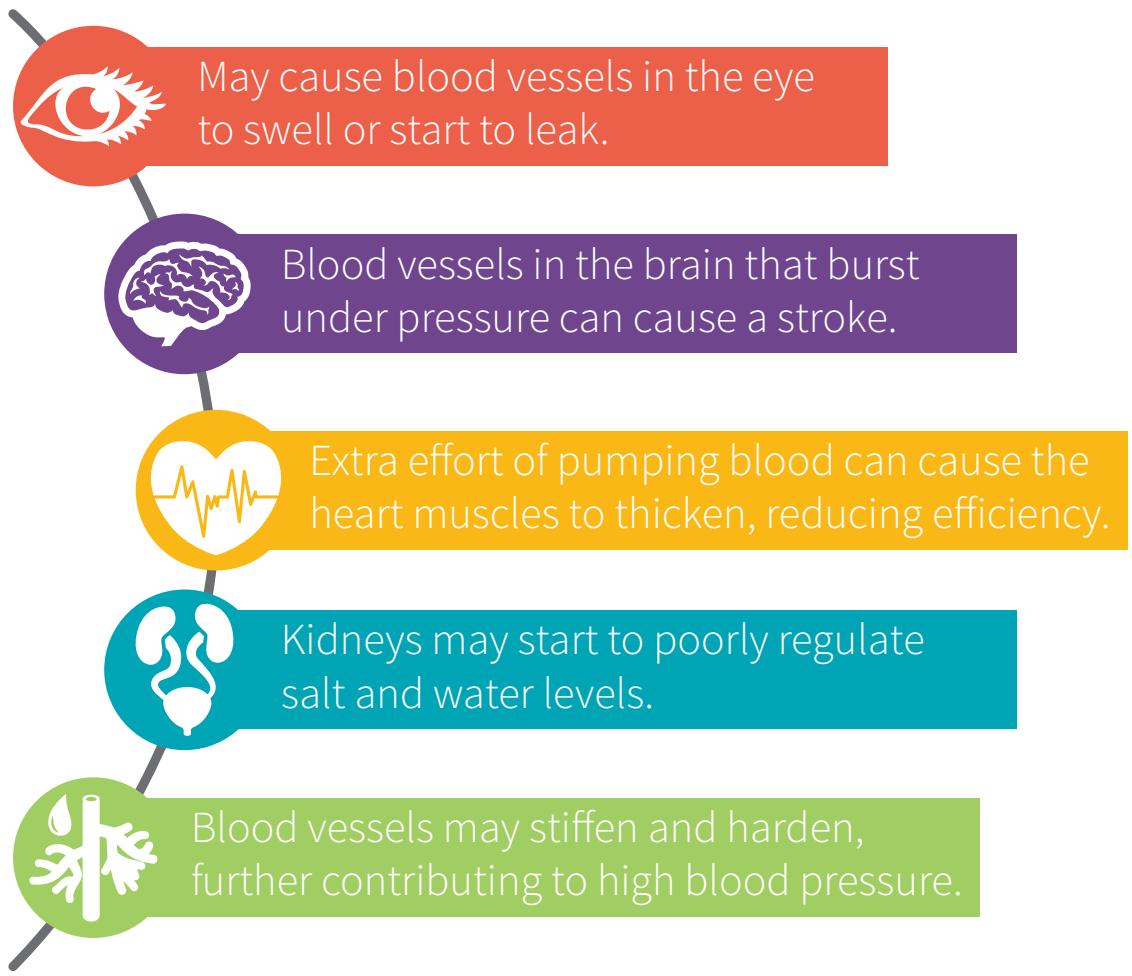
High blood pressure, or hypertension, is one factor that contributes significantly to cardiovascular disease (CVD). Blood pressure is usually reported in two numbers. For example, a reading of 120/80 mm Hg. The first number, systolic blood pressure, tells us how much pressure your blood is exerting against the arterial walls when your heart contracts. The second number signifies how much pressure your blood is exerting when the heart is relaxed and being refilled with blood. Blood pressure is generally divided into four categories:

- Normal - ≤120/80
- Prehypertension – 120-139/80-89
- Hypertension Stage 1 – 140-159/90-99
- Hypertension Stage 2 – ≥160/100

For people with hypertension or those who take blood pressure-lowering medication, the lifetime risk at age 30 for developing CVD is 37.3% higher than for people with normal blood pressure (absolute risk of 46.1% vs. 63.3%). These patients with hypertension also developed CVD five years earlier, comparatively. Chronic high blood pressure also creates health concerns (detailed in Figure 1) such as increased risk of stroke and organ damage.

Clinically, even a small two to five mm Hg decrease in systolic blood pressure can noticeably reduce CVD and total mortality. Observational trials have demonstrated mixed results when looking at associations between increased protein intake and a decrease in blood pressure. But RCTs have more consistently shown a modest benefit - particularly when the protein intake offsets some carbohydrate in the diet. Dairy foods, in addition to their protein content, may be able to provide additional benefits through their nutrient profile, which could further help reduce blood pressure. Getting adequate amounts of calcium, magnesium, and potassium can also reduce blood pressure. Dairy products can be a good source of all three. Furthermore, dairy intake seems to correlate with small reductions in blood pressure. Since milk contains both protein and minerals,

Figure 1: Complications of high blood pressure



this raises the question of whether the protein in milk alone could lead to these reductions. The present study sought to further investigate the potential acute and chronic effects of two common dairy proteins, whey and calcium caseinate (Ca caseinate), on blood pressure and vascular function in people with high blood pressure.

High blood pressure is a large contributing factor to CVD that could see potential mitigation through increased protein intake. The present study examines the acute and chronic effects of whey and casein on blood pressure and vascular function in people with high blood pressure.

Who and what was studied?

The trial was a double-blinded, randomized, three-way-crossover, controlled intervention study. Forty-two nonsmoking men and women with pre- or hypertension (120/80-159/99 mm Hg) were recruited for the study. The average age was 53 and average BMI was 27, placing most subjects in the 'overweight' category. All participants underwent three separate eight-week intervention periods that were each separated by a four-week washout period. The three eight-week interventions were:

- Two doses of 28 grams of whey protein isolate, a fast digesting protein, per day
- Two doses of 28 grams of Ca caseinate, a slower digesting protein, per day
- Two doses of 27 grams of maltodextrin, a refined carbohydrate supplement (control), per day

The order in which participants undertook these intervention periods was randomly assigned to help prevent any bias of a carry-over effect. A carry-over effect is if one intervention "carries over" to the next and confounds the results. The four-week washout period between interventions also aimed to reduce this effect.

The researchers attempted to add in the various supplements on top of the participants' usual diets without significantly altering their standard intake. Thus, all participants received dietary counseling on how to incorporate the study drinks without substantially altering typical caloric intake, macronutrient composition, or food choices. Moderate changes in diet can affect blood pressure, so the researchers wanted to ensure no significant dietary changes were being made over the course of the trial.

The primary outcome of the study was change in 24-hour ambulatory blood pressure (24-h AMBP), the gold standard in blood pressure measurements. This is achieved by having the participants wear a device that checks their blood pressure at frequent regular intervals throughout the day and night. Blood pressure measurements from clinic visits were also assessed. These were done via automated BP monitor, which took measurements every five minutes, up to 30 minutes. The secondary outcomes included a measure of vascular function measured by flow-mediated dilation (FMD), changes in plasma lipids, markers of insulin resistance (fasting glucose, HOMA-IR), inflammatory markers (CRP, IL-6, TNF-α), and arterial stiffness.

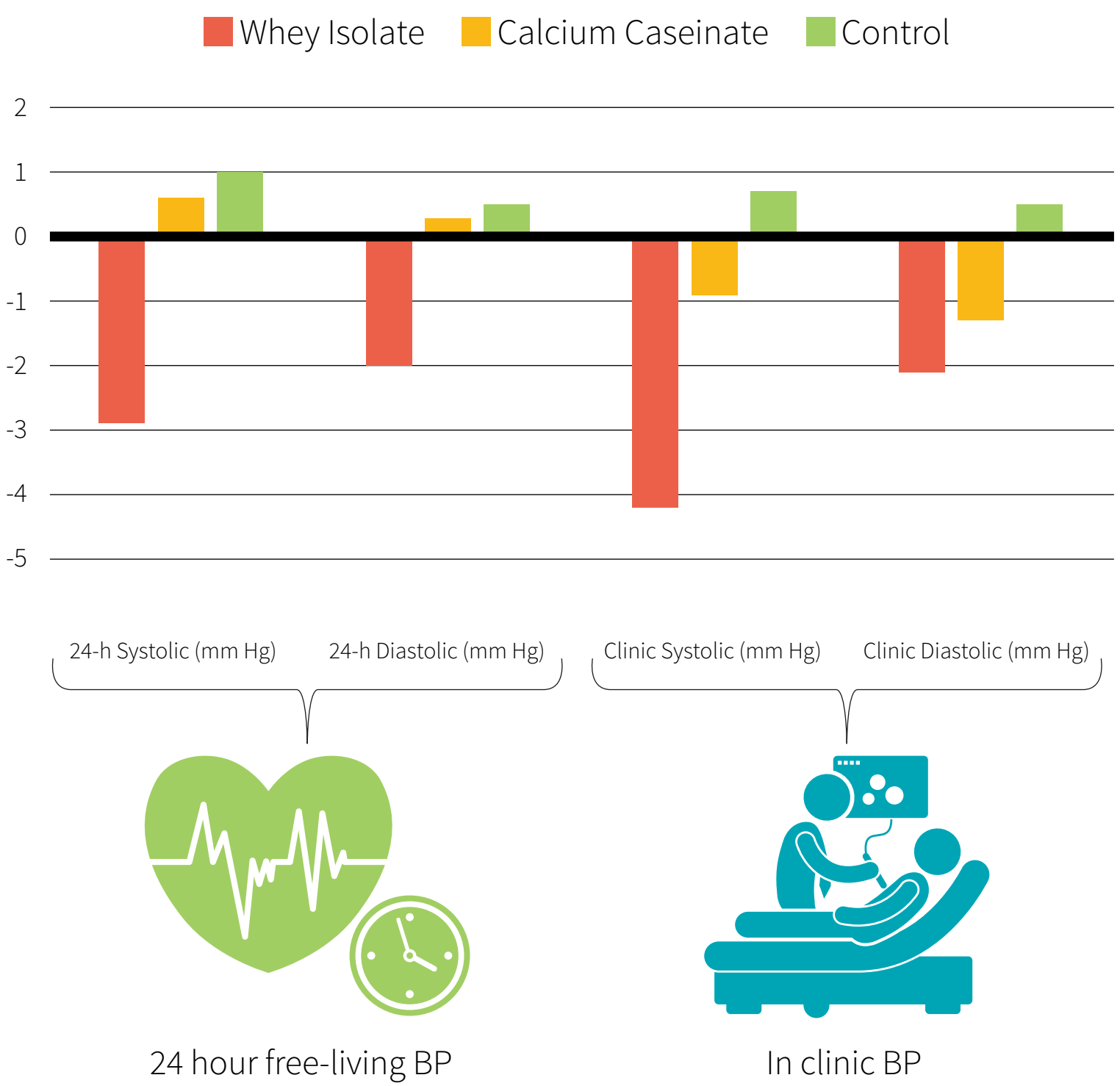
Forty-two participants with pre-hypertension or hypertension were enrolled into this double-blinded, randomized, three-way-crossover, controlled intervention study. The study was made up of three eight-week interventions, each separated by a four-week washout period. All participants undertook all three interventions during the study. The three interventions consisted of twice daily supplementation of 28 grams of whey protein isolate, 28 grams of Ca caseinate, or 27 grams of maltodextrin (control). The primary outcome was change in 24-hour ambulatory blood pressure. Secondary outcomes were changes in vascular reactivity, lipids, markers of insulin resistance, inflammatory markers, and arterial stiffness.

What were the findings?

Four participants dropped out of the trial (9.5% drop-out rate), three due to a dislike of the taste of the whey and caseinate drinks, while one simply lost interest. Thirty-eight participants were included in the final analysis. Compliance was high among all three interventions, with about 90% of all supplements being taken in each intervention period. BMI, weight, lean body mass, and fat mass did not significantly change over the course of the study, as measured via bioelectrical impedance (BIA) scale, reducing the effects that weight loss or gain may have on BP. No effect on nutrient intakes were observed apart from the increased protein intake for both protein intervention groups, the increased calcium intake for the Ca caseinate group, and the increased carbohydrate in the control group.

Figure 2 shows some of the main study findings. For the primary outcome measure of 24-h AMBP, there was a significant overall effect in the whey isolate group, but the changes were small. The whey intervention saw a -2.9 mm Hg reduction in 24-h systolic blood pressure and -2.0 mmHg reduction in 24-h diastolic blood pressure. Ca caseinate and placebo both saw small increases in both these measures, but the former was statistically equivalent to whey due to noise. The in-clinic tests of BP also saw a significant treatment effect for systolic

Figure 2: Changes in blood pressure from baseline



blood pressure (-4.2 mmHg), but not diastolic blood pressure, in the whey protein intervention when compared to placebo.

Vascular function improved in both protein interventions but worsened in the control group. Arterial stiffness saw no difference between groups. Total cholesterol was decreased with use of either protein, though. None of the interventions had any significant effect on markers of insulin resistance, sensitivity, or on any inflammatory markers.

Study compliance was high and the dropout rate was low. No major changes in body composition or diet were seen for the duration of the trial. Overall, the whey protein group experienced the greater reductions in blood pressure. Vascular function and cholesterol improved in both protein groups over placebo. No significant changes were seen in insulin resistance, sensitivity, or inflammatory markers.

What does the study really tell us?

This study demonstrates that use of a whey protein at a dose of 56 grams a day for eight weeks can yield clinically relevant reductions in systolic and diastolic blood pressure compared to a placebo in people with pre- or hypertension. While the Ca caseinate supplement did yield some results that trended toward significant over placebo, they were less pronounced than what was seen while using whey protein.

One major benefit of this study over prior trials was the use of 24-h AMBP devices to get a more accurate reading of blood pressure over time compared to measuring BP just on clinic visits or having participants sporadically measure their BP over the course of a day. Measures of BP in a clinic may be confounded due to the so-called "white-coat effect," when patients may experience higher than normal blood pressure due to the anxiety of being in a doctor's office or because of apprehension about the test itself.

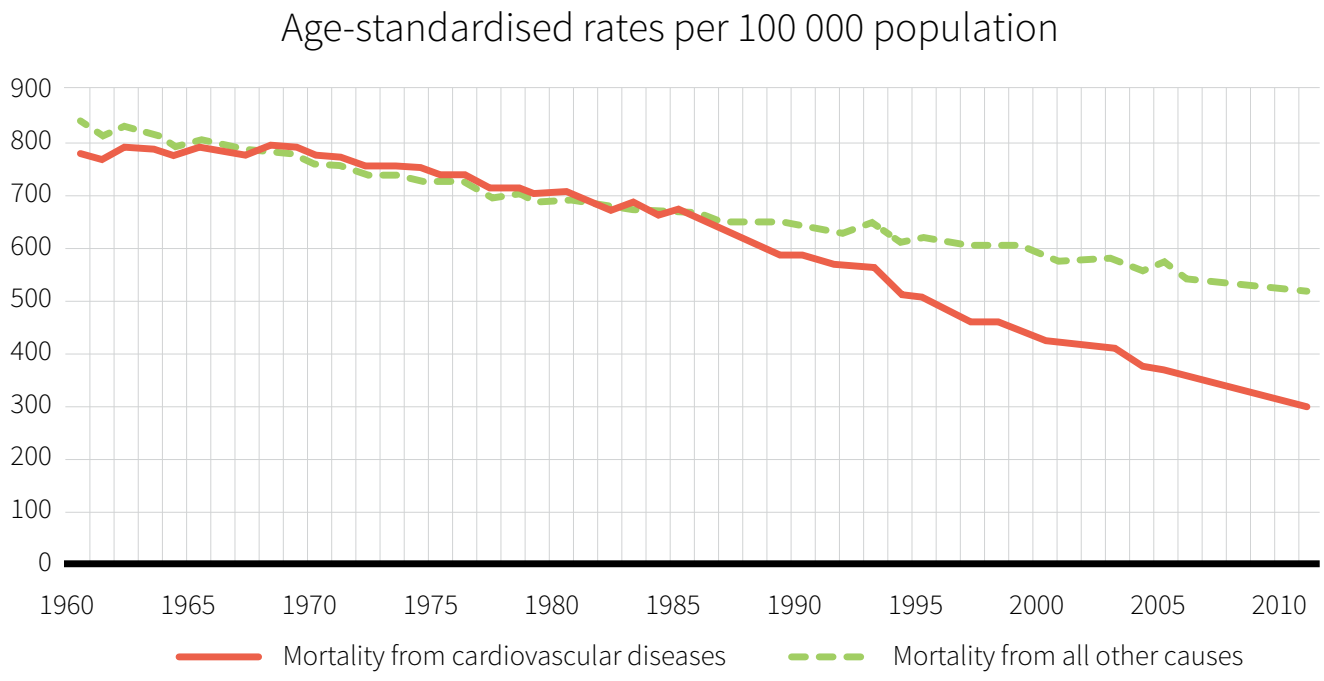
A curiosity of the study was that, although calcium intake has been associated with decreases in BP, the Ca caseinate supplement did not have a significant effect on BP despite having a calcium content 2.5-fold higher than whey protein. This indicates that participants were already getting sufficient amounts of calcium in their diet and/or that the protein supplements are acting through different mechanisms to yield blood pressure reductions.

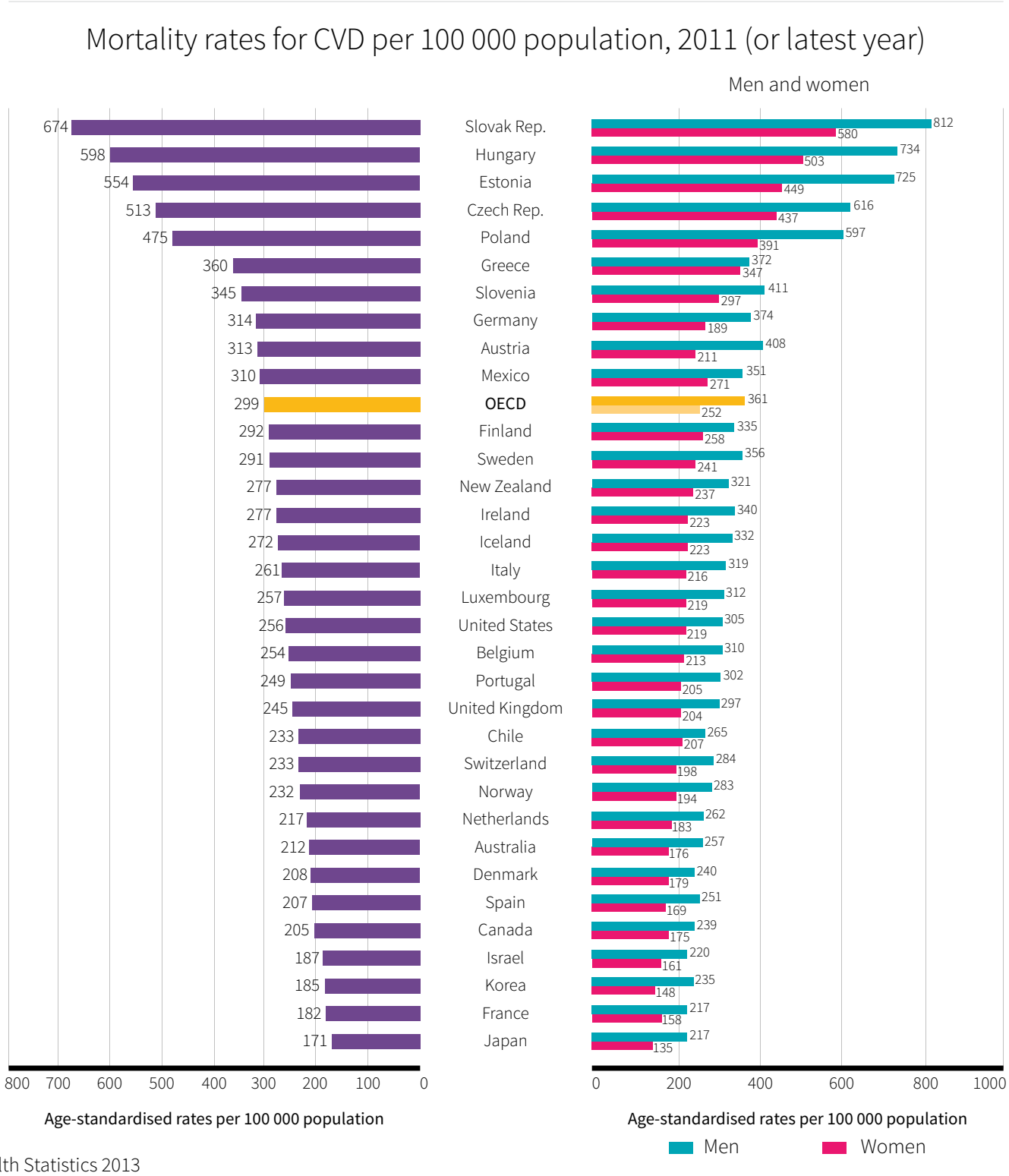
There's an additional important factor here to consider here. The control group was given 54 total grams of maltodextrin a day adding 216 calories of a refined carbohydrate to their diet per day. So they were comparing protein supplements versus a highly refined carbohydrate control group, which may increase the likelihood of obtaining a favorable result for the protein groups. It would have been helpful to have a fourth group that didn't receive anything, or a non-nutritive supplement that added no calories to their diet.

Of note is that, while the study was not funded by a corporation, Volac International Ltd. provided the supplements used in the study and two of the authors have previously worked with the dairy industry.

There are limitations to the general applicability of the research findings. This study population was an otherwise healthy group who already had existing pre- or hypertension. Individual results may vary depending on how close or far away your personal health situation relates to the participants in this study. As shown in Figure 3, cardiovascular disease varies substantially across different countries, and it's hard to know what impact interventions would have in different types of people.

Figure 3: Mortality rates for cardiovascular diseases and all other causes of death in OECD countries





Source: OECD Health Statistics 2013

A high daily dose of whey protein can produce clinically relevant reductions in blood pressure over at least an eight-week period. While the Ca caseinate did produce some favorable changes, those in the whey group experienced a more pronounced effect. The results of the study are strengthened by its use of the of 24-h AMBP devices, which provide more accurate results than more commonly used methods, such as in-clinic only testing.

The big picture

While some observational studies and most RCTs have shown a benefit to BP with higher protein intake (from both plant and animal sources), the authors of the study under review noted an important limitation of their study and the body of research at large in this area. They state, "[A] potential limitation was that the daily dose given in this trial was relatively high [at 56 grams a day], and therefore further studies are required to determine the lowest effective dose...". Indeed, studies have not established a minimum dose needed to see these effects, or whether the larger protein intake might lead to greater reductions in blood pressure.

When examining the data we have from RCTs, the overall effect of increased protein on blood pressure is small - typically amounting to a 2-3 mm Hg reduction in overall BP. While this can help, a more comprehensive approach will be needed for most to get their BP back into a healthy range, such as increased fruit and vegetable intake and the inclusion of some form of aerobic exercise. Effects of blood pressure from various lifestyle modifications are detailed in the FAQ section below.

If you are considering an increase to your protein intake through whole food sources or supplements as part of a larger strategy to help manage your blood pressure, aim for sources that will not add a lot of excess fat or carb calories to your diet as to cause weight gain - a factor that will act as a detriment to decreasing BP.

The effects of increased protein intake on BP are very small. A more comprehensive lifestyle modification will be needed for many to get their blood pressure back into a healthy range. If you intend to increase protein as part of a larger overall strategy, aim for lower-calorie protein sources to minimize adding excess fat and carb calories to your diet.

Frequently asked questions

How does an increased protein intake compare to other treatment options for high blood pressure?

Hypertension can be handled using a multitude of approaches which are often better in combination than they are in isolation. However, here are how the individual treatments can affect your blood pressure by themselves:

- Increased protein intake (minimum effective dose unknown) - 2 to 3 mm Hg

> "It does appear that both vegetable and animal protein sources can significantly reduce blood pressure."

- Losing weight (if BMI > 24.9) - 5 to 20 mm Hg per 10 kg (22 lbs) weight loss
- DASH diet rich in fruits and vegetables, lower in fat and saturated fat - 8 to 14 mm Hg
- Reducing sodium intake - 2 to 8 mm Hg
- Increased physical activity, especially aerobic activity - 4 to 9 mm Hg
- Reduction in alcohol consumption to moderate levels or below - 2 to 4 mm Hg

Can other non-dairy sources of protein also reduce blood pressure?

It does appear that both vegetable and animal protein sources can significantly reduce blood pressure. A meta-analysis examining the effects of dietary protein intake noted that, regardless of the source, participants were able to experience a reduction of a least 2.0 mm Hg in systolic pressure and about a 1.0 mm Hg reduction in diastolic pressure, on average. The authors mentioned that swapping out some carbs for protein in the diet may be the best route for seeing these effects.

What should I know?

The present study is consistent with previous research that increasing protein intake can reliably produce a small decrease in blood pressure. However, manipulating protein intake alone is unlikely to be sufficient by itself to bring BP back into a healthy range in those with pre- or hypertension. Other lifestyle factors, such as smoking cessation, moderation of alcohol intake, increased activity level, and attention to diet quality are more likely to yield a synergistic beneficial effect on BP, lowering the odds of developing CVD. ◆

The strongest implication of this study may to replace beverages high in refined carbs with protein shakes, if you need to lower your blood pressure. Discuss this topic further at the ERD Facebook forum.