Sex differences in response to dietary manipulation in rats with hypertension and myocardial hypertrophy1–3

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ABSTRACT Studies of the effect of sex on the metabolic state of rats with chronic hypertension and concomitant myocardial hypertrophy were conducted. Female and male spontaneously hypertensive rats (SHRs) with early myocardial hypertrophy (5.5 mo old) were used. Serum fatty acids, liver glycogen, and myocardial glycogen were measured at baseline and after the rats were deprived of food for 24 h. The metabolic effects of progressive myocardial hypertrophy in females were assessed in additional groups of female SHRs (5.5 or 12 mo old) under the following conditions: control, food deprived, or food deprived and refed with equienergetic lipid-rich (38.9% of total energy) or carbohydrate-rich (76.5% of total energy) diets. Despite no differences in serum fatty acids, females had significantly higher baseline myocardial glycogen and liver glycogen concentrations than males. In response to food deprivation, females continued to have significantly higher myocardial glycogen and fatty acid concentrations than males, whereas there were no sex differences in liver glycerogen, which was depleted in both males and females. Older hypertensive females had higher baseline fatty acid concentrations and lower liver glycogen concentrations than younger females, whereas there were no differences in myocardial glycogen. Food deprivation doubled fatty acid concentrations, depleted liver glycogen, and increased myocardial glycogen in both age groups. In both age groups, fatty acid concentrations and liver glycogen did not return to baseline values after food deprivation and refeeding. In both age groups, fatty acid concentrations increased further after the lipid-rich diet whereas liver glycogen concentrations returned to ~50% of baseline values whereas the carbohydrate-rich diet. Refeeding with either diet did not significantly increase myocardial glycogen further. Thus, the metabolic response to dietary manipulation was influenced by both sex and, in females, progressive pathology. Am J Clin Nutr 1997;66:1428–1435.

KEY WORDS Sex, myocardial hypertrophy, myocardial glycogen, liver glycogen, spontaneously hypertensive rats, food deprivation, refeeding, fatty acids

INTRODUCTION Evidence from animal and human studies suggests that myocardial hypertrophy associated with chronic hypertension is more prevalent in females than in males, and that once a positive diagnosis of congestive heart failure has been made the duration of survival is shorter in females (1–3). Patients are in a variety of nutritional states before either surgery or any number of medical interventions. Food deprivation is required in these patients for short periods, which is often followed by a regimented diet.

Nutritional status has well-documented effects on metabolism in a variety of organs. In response to food deprivation, these effects include mobilization of liver glycogen and lipids from adipose tissue in the form of fatty acids (4). Interestingly, in contrast with the response in the liver, myocardial glycogen in both normal and hypertrophied hearts increases after food deprivation (5–8). Both liver glycogen and myocardial glycogen increase in response to increased dietary carbohydrate and fat intakes (7).

The role of sex in these dietary responses is not clear. It has been reported that in response to prolonged food deprivation, female rats with normal hearts have higher fatty acid and plasma ketone concentrations and lower plasma glucose concentrations than males (9). However, the metabolic response of individuals with hypertension or myocardial hypertrophy to such manipulation, and whether there are differences between males and females in these responses, is unknown. Hypertrophied hearts tolerate ischemia less well than do normal hearts in humans (10, 11) and in various animal models (12–15), due, in part, to decreased energy reserves (14). High myocardial glycogen concentrations in normal hearts improve tolerance to ischemic insult by prolonging anaerobic energy production in a variety of species, including humans (16, 17) and rats (18). Therefore, interventions that increase myocardial glycogen may be cardioprotective.

The current study compared the metabolic profiles of age-matched male and female rats with chronic hypertension and concomitant myocardial hypertrophy with those that endured short-term food deprivation. In addition, to determine whether the degree of pathology affected female metabolic responses to dietary manipulation (food deprivation or food deprivation and refeeding with various diets), females of two different ages were studied. Spontaneously hypertensive rats (SHRs), a model...
of pressure-overload-induced hypertrophy, were used to mimic essential hypertension in humans.

MATERIALS AND METHODS

Male SHRs aged 5.5 mo and female SHRs aged either 5.5 mo with early hypertrophy (EH) or 12 mo with more advanced hypertrophy (AH) were studied. Male rats were allocated into one of two groups: control rats fed a commercial nonpurified diet (Purina Rat Chow 5012; Ralston Purina Canada Inc., Chomedey, Canada) ad libitum (n = 27), or rats food-deprived for 24 h before being killed (n = 28). Female rats with EH and AH were allocated into one of four groups according to the dietary manipulation they underwent: controls fed the commercial nonpurified diet ad libitum (EH, n = 37; AH, n = 25), rats food-deprived for 24 h before being studied (EH, n = 58; AH, n = 19), and rats food-deprived for 24 h and then refed equienergetically for 1 h with the commercial nonpurified diet supplemented with either dextrose (EH, n = 10; AH, n = 4) or safflower oil (EH, n = 10; AH, n = 4). The composition of each diet according to the source of energy is shown in Table 1. The rats were housed individually under similar conditions and were treated in accordance with the guidelines of the National Institutes of Health and the Canadian Council on Animal Care.

After the period of food deprivation or food deprivation and refeeding, the rats were studied. In a subset of rats of each sex and age, the right carotid artery was cannulated after anesthesia was induced with Inactin (100 mg/kg intraperitoneally; Research Biochemicals International, Natick, MA) to allow measurement of baseline arterial blood pressures with the Biopac MP100 and AcqKnowledge software (Biopac Systems, Goleta, CA). Samples of blood, liver, and myocardium were taken from all animals. Baseline plasma glycogen concentrations in rats not deprived of food were measured by using the Accu-chek system (Boehringer Mannheim Ltd, Laval, Canada). Serum was separated and analyzed for fatty acid content according to the method of Duncombe (19). Myocardial and liver glycogen were measured by spectrophotometry using methods described by Good et al (20). The myocardial DNA content in females was determined by using the method of Schneider (21).

Data are expressed as means ± SEMs. Student’s t test was used to compare DNA between 5.5- and 12-mo-old females. Two-way analysis of variance (ANOVA) was used to compare metabolic indexes in response to treatments and sex and across ages in response to dietary manipulation (22). Differences were specified by using the contrast procedure post hoc. All statistics were calculated by using Statistical Analysis System (SAS) software (version 6.08; SAS Institute Inc, Cary, NC). Statistical significance was accepted at P < 0.05.

**RESULTS**

**Rats with hypertension and early hypertrophy: males compared with females**

There were no significant sex differences in either mean arterial pressures (males: 186.3 ± 5.5 mm Hg; females: 179.6 ± 2.5 mm Hg) or plasma glucose concentrations (males: 6.5 ± 0.4 mmol/L; females: 6.6 ± 0.5 mmol/L).

Myocardial glycogen, liver glycogen, and serum fatty acid concentrations of age-matched male and female 5.5-mo-old SHRs under control and food-deprived conditions are shown in Figure 1. Baseline myocardial glycogen and liver glycogen were significantly lower in male than in female control rats (P < 0.0001), whereas there were no significant differences in fatty acid concentrations. Food deprivation increased myocardial glycogen by 90% in males (P < 0.05) but by only 29% in females (P < 0.001), whereas fatty acid concentrations increased by 52% in males (P < 0.001) and by as much as 160% in females (P < 0.01). Food deprivation dramatically reduced liver glycogen in both sexes (P < 0.0001), by 87% in males and 95% in females.

In response to food deprivation, females had higher serum fatty acid concentrations than males (P < 0.001) whereas liver glycogen fell to similar concentrations despite significant sex differences at baseline. Although males experienced greater increases in myocardial glycogen in response to food deprivation, they continued to have lower myocardial glycogen concentrations than females (P < 0.0001).

In summary, female SHRs had significantly higher baseline liver glycogen and myocardial glycogen concentrations than males but had higher serum fatty acid concentrations and a depressed ability to increase myocardial glycogen in response to food deprivation for 24 h compared with age-matched males.

**Rats with hypertension and early compared with advanced hypertrophy: females**

**Baseline**

No significant differences were seen between 5.5-mo-old and 12-mo-old female SHRs in either mean arterial pressures (5.5 mo: 179.6 ± 2.5 mm Hg; 12 mo: 180.1 ± 6.1 mm Hg) or plasma glucose concentrations (5.5 mo: 6.6 ± 0.5 mmol/L; 12 mo: 5.8 ± 0.5 mmol/L).

Tissue DNA concentrations was used to assess the degree of hypertrophy. Older female rats had lower myocardial DNA concentrations (1.41 ± 0.07 μg/mg myocardium) than younger females (1.80 ± 0.06 μg/mg myocardium, P < 0.0001), indicating that older hearts had a significantly greater degree of hypertrophy. Females of both ages had substantially lower DNA concentrations than those seen previously in males with nonhypertrophied hearts (2.58 ± 0.10 μg/mg myocardium) (6).

Baseline serum fatty acid concentrations were significantly higher (P < 0.001) and liver glycogen significantly lower (P < 0.001) in older than in younger females, whereas no significant age difference in myocardial glycogen was seen (Table 2).

**Food deprivation**

Food deprivation produced dramatic changes in all measured indexes compared with baseline values (Table 2). In both age groups, fatty acid concentrations of food-deprived rats increased to twice those of controls, with older female rats
having significantly higher ($P < 0.01$) fatty acid concentrations than younger females. Liver glycogen concentrations were depleted in response to food deprivation in both 5.5- and 12-mo-old female rats, by 95% and 92%, respectively. Food deprivation increased myocardial glycogen above baseline in both age groups, by 29% and 19%, respectively. Despite higher serum fatty acid concentrations in older females that had been food deprived, there were no significant age differences in liver glycogen and myocardial glycogen concentrations in food-deprived rats.

**Food deprivation and refeeding**

In older females, refeeding with the dextrose-supplemented diet resulted in fatty acid concentrations (0.46 ± 0.06 g/L) that were lower, but not significantly so, than those in rats either food deprived only or those food deprived and re-fed oil (0.84 ± 0.14 g/L) (Figure 2). In 5.5-mo-old females, rats deprived of food and re-fed a supplemented diet had serum fatty acid concentrations greater than those in rats food deprived only, although only significantly so in the oil-refed group. The oil-refed younger females (0.73 ± 0.19 g/L) had significantly higher ($P < 0.001$) values than the dextrose-supplemented females (0.34 ± 0.07 g/L). Serum fatty acid concentrations remained significantly increased above baseline concentrations in both dextrose- and oil-refed animals in both age groups.

In 12-mo-old females, rats re-fed with the dextrose-supplemented diet had liver glycogen concentrations greater than those of rats food deprived only ($P < 0.001$). In 5.5-mo-old females, liver glycogen concentrations after both the dextrose- ($P < 0.001$) and oil- ($P < 0.05$) supplemented diets were higher than those after food deprivation only. In 12-mo-old female rats, liver glycogen concentrations returned to 50% (74.35 ± 12.47 μmol/g wet wt, $P < 0.001$) of baseline concentrations after the dextrose-supplemented diet and to 52% of baseline concentrations after the oil-supplemented diet (78.26 ± 11.18 μmol/g wet wt, $P < 0.05$) (Figure 3).

**TABLE 2**

Metabolic profiles of female spontaneously hypertensive rats

<table>
<thead>
<tr>
<th>Time of measurement and age</th>
<th>Fatty acids</th>
<th>Liver glycogen</th>
<th>Myocardial glycogen</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>g/L</td>
<td>μmol/g wet wt</td>
<td>μmol/g wet wt</td>
</tr>
<tr>
<td>Baseline</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5.5 mo ($n = 37$)</td>
<td>0.11 ± 0.01</td>
<td>215.88 ± 9.46</td>
<td>11.10 ± 0.41</td>
</tr>
<tr>
<td>12 mo ($n = 25$)</td>
<td>0.28 ± 0.02</td>
<td>150.41 ± 10.28</td>
<td>11.34 ± 0.71</td>
</tr>
<tr>
<td>After food deprivation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5.5 mo ($n = 58$)</td>
<td>0.30 ± 0.04</td>
<td>10.12 ± 2.18</td>
<td>14.34 ± 0.55</td>
</tr>
<tr>
<td>12 mo ($n = 19$)</td>
<td>0.59 ± 0.13</td>
<td>12.28 ± 6.25</td>
<td>13.51 ± 0.74</td>
</tr>
</tbody>
</table>

1. $\bar{x}$ ± SEM.
2. Significantly different from 5.5 mo, $P < 0.05$.
3. Significantly different from baseline, $P < 0.05$.
oil-supplemented diet (56.58 ± 8.75 μmol/g wet wt, \( P < 0.001 \)). Thus, refeeding was more effective in restoring liver glycogen concentrations depleted by food deprivation in older rats than in younger rats, with the dextrose-supplemented diet resulting in the greatest repletion.

In 12-mo-old female rats, refeeding increased myocardial glycogen concentrations above those after food deprivation only, by 21% with the dextrose-supplemented diet (16.32 ± 1.87 μmol/g wet wt; NS) and by 24% with the oil-supplemented diet (16.74 ± 1.95 μmol/g wet wt; NS) (Figure 4). In older female rats, myocardial glycogen concentrations increased significantly above baseline values by 44% after the dextrose- \(( P < 0.05 \)) and by 48% after the oil- \(( P < 0.01 \)) supplemented diets. Similar increases \(( P < 0.001 \)) above baseline were seen in the younger females: 44% after the dextrose- and 49% after the oil-supplemented diets. These increases were 11–15% above those after food deprivation only (NS).

Overall, significant metabolic differences were seen between 5.5- and 12-mo-old female SHR rats under baseline conditions, whereas both age groups responded similarly to food deprivation for 24 h. Despite these differences in baseline values, age did not influence the response of specific profiles to refeeding with supplemented diets, but did alter the magnitude of the change from baseline values and those after food deprivation.

**DISCUSSION**

Studies of patients and animals show that for similar degrees of hypertension, a greater magnitude of myocardial hypertrophy develops in females than in males (1, 2, 23, 24). A strong association exists between the incidence of hypertension and congestive heart failure in women, as well as shorter survival times for women once a positive diagnosis has been made (3). Nutritional status can have dramatic effects on morbidity and mortality in heart patients. For example, high serum fatty acid concentrations increase the incidence of arrhythmias and decrease heart function (25, 26). Therefore, nutritional manipulation could have a dramatic effect on patients with coronary artery disease. Because females with essential hypertension may be at greater risk from existing coronary artery disease than males, the effects of sex on systemic and myocardial responses to dietary manipulation were studied. In an SHR model, for similar degrees of systemic hypertension, there were significant sex differences in the same age groups and significant age differences within females. These differences are discussed in relation to specific changes in plasma and organ metabolites.

**Serum fatty acid concentrations**

Food deprivation induced a shift from carbohydrate to lipid metabolism, because of mobilization of liver glycogen fol-
alyzed by the release of fatty acids from adipose tissue. Despite similar baseline serum fatty acid concentrations between males and females, females had significantly higher liver glycogen concentrations, suggesting that females with hypertension and myocardial hypertrophy have an altered carbohydrate metabolism compared with age-matched males. After being deprived of food for 24 h, female rats had less of an increase in serum fatty acid concentrations and a greater depletion of liver glycogen than male rats, lending further support to an increased reliance on carbohydrates in females.

Interestingly, serum fatty acid concentrations in 12-mo-old female SHRs were double those of the 5.5-mo-old female rats under both control and food-deprived conditions. Higher serum fatty acid concentrations in older females may indicate that the ability to transport lipids across cell membranes decreases with age, or that the activity of lipoprotein lipase is enhanced with age. Serum fatty acid concentrations impair hepatic insulin extraction, leading to reduced glucose utilization by the liver, an effect that would be exacerbated by higher fatty acid concentrations. Alternatively, because it is known that advanced coronary artery disease and myocardial hypertrophy can result in cardiac cachexia, older females with more advanced myocardial hypertrophy may be in a state of nutritional stress similar to food deprivation. However, the experimental protocol used ensured that animals in both age groups were fed equienergetically; thus, no difference in food consumption occurred, eliminating this as a possible explanation for the observed age-related differences in fatty acid concentrations.

The doubling of serum fatty acid concentrations in response to food deprivation in both 5.5- and 12-mo-old female SHRs agrees with results from studies in female Wistar rats (9).

In both age groups of female rats, refeeding did not result in a return of serum fatty acid concentrations to baseline concentrations. In fact, the increase in fatty acid concentrations as a result of food deprivation alone was exacerbated by the oil-rich diet in both 5.5- and 12-mo-old SHRs. Refeeding the dextrose-enriched diet either did not further increase fatty acid concentrations above values after food deprivation only, or, in 12-mo-old females, resulted in a 22% decrease. Clearly, serum fatty acid concentrations require a longer time to return to baseline concentrations after food deprivation and refeeding than was provided for in this study. This sustained increase in serum fatty acid concentrations may have serious implications in female patients susceptible to cardiac arrhythmias or decreased cardiac function.

Liver glycogen

As discussed previously, both 5.5-mo-old males and 12-mo-old females had lower liver glycogen concentrations than 5.5-mo-old females, indicating a possible decrease in substrate uptake. Indirect evidence for a possible decrease in substrate uptake was shown by the lower baseline liver glycogen concentrations in 12-mo-old female SHRs than in 5.5-mo-old female rats, despite similar baseline plasma glucose concentrations. This suggests that older females with low liver glycogen reserves, possibly because of a decreased production-to-use

![Liver glycogen concentrations](https://academic.oup.com/ajcn/article-abstract/66/6/1428/4655986/fig3.png)
ratio, may have a more restricted capacity to maintain stable blood glucose concentrations under conditions of significant metabolic stress. The greater baseline fatty acid concentrations and lower baseline liver glycogen concentrations in older than in younger female SHRs may indicate that a prolonged disease state (hypertension or hypertrophy) predisposes females to altered substrate handling. This implies that whole-body metabolism is altered with the progression of hypertension. Depressed liver glycogen may signify that carbohydrates are the major fuel source for older females, such that fatty acid concentrations are not being converted into triacylglycerols by the liver.

Intriguingly, food deprivation reduced liver glycogen to similar concentrations in both age groups of female SHRs despite significant differences in baseline values. Thus, the ability to fully mobilize stored liver glycogen in an attempt to maintain blood glucose concentrations in response to metabolic stress was preserved in the older hypertensive females, despite the lower reserves.

Compared with baseline, refeeding with the dextrose-enriched diet increased liver glycogen concentrations more than did the oil-rich diets, possibly because carbohydrates are more efficiently converted to glycogen than to lipids (27). Despite these increases in both 5.5- and 12-mo-old female rats, liver glycogen returned to only 50% of baseline concentrations in either refed group. A longer refeeding time may therefore be required for liver glycogen concentrations to completely return to baseline concentrations. A carbohydrate-enriched diet appears to be the best method to reduce the harmful systemic effects of food deprivation because serum fatty acid concentrations increased less than with oil, whereas liver glycogen repletion was greater.

Myocardial glycogen

Within the context of these systemic effects, the effect of dietary manipulation on myocardial glycogen in light of myocardial hypertrophy must be considered. The heart can metabolize a variety of substrates to meet its energy requirements, depending primarily on serum substrate concentrations. Although fatty acids are the preferred substrate of a normal adult heart, both exogenous glucose and endogenous glycogen can be utilized by the myocardium if necessary. Significant increases in myocardial glycogen in response to food deprivation in normal hearts were observed > 60 y ago (28). The glycogen concentration in the heart increases in response to two metabolic effects of food deprivation: inhibitory effects of lipolysis on glycolysis and glycogenolysis, and competition for carrier compounds (such as coenzyme A) common to both lipid and carbohydrate metabolic pathways (8).

Pressure-overload myocardial hypertrophy is associated with an increased reliance on glycolytic energy metabolism (29); thus, increases in myocardial glycogen in this population may be even more beneficial than in nonhypertrophied hearts. Because of the potential cardioprotective effect of myocardial glycogen and the established relation between nutritional status and myocardial glycogen concentration, the sex-specific nature of the metabolic response to dietary manipulation may provide sex-specific benefits. Significantly higher baseline liver glycogen and myocardial glycogen concentrations in females than in age-matched males may protect females from metabolic stress.
Estrogen has well-established effects on carbohydrate metabolism, including increased pancreatic insulin secretion and improved peripheral insulin sensitivity (30). Górski et al (31) found that estradiol administration to ovariectomized rats without existing cardiovascular pathology resulted in increased myocardial glycogen recovery and delayed liver glycogen mobilization in response to prolonged exercise. Increased glucose uptake in females due to the influence of estrogen could explain the higher baseline myocardial glycogen and liver glycogen concentrations seen in the present study.

In the presence of myocardial hypertrophy, the magnitude of the increase in myocardial glycogen in response to food deprivation was much greater in male (90%) than in age-matched female (29%) rats. This suggests that females with hypertrophy have a decreased ability to increase myocardial glycogen, possibly because of sex-specific alterations in enzyme activities associated with the pathology. These results are similar to those reported by Arnall et al (9), who showed that in normotensive, non-hypertrophied rats, food deprivation produced a significant increase in myocardial glycogen in male rats (31%), whereas female rats showed no increase. Thus, in both pathologic and nonpathologic states, males clearly have a greater ability to increase myocardial glycogen reserves than do females. The enhancing effect of systemic hypertension and hypertrophy on the myocardial glycogen response to food deprivation may explain the lack of effect observed by Arnall et al. In the absence of these pathologic conditions, the females used in Arnall et al’s study showed no response to food deprivation, whereas the current study showed a significant effect in females with these pathologic conditions. Interestingly, in both Arnall et al’s normal rats and rats with hypertension and myocardial hypertrophy, the depressed ability of females to increase myocardial glycogen indicates that sex exerts a major effect, which is exacerbated by the presence of hypertrophy.

There is a well-documented relation between the presence of hypertension and decreased insulin-stimulated glucose uptake in both animal models and humans (32). This may predispose hypertensive animals to lower tissue glycogen concentrations compared with normotensive animals. It may also explain why the increase in myocardial glycogen in response to food deprivation for 24 h in both male and female SHRs was less than that reported previously in normotensive rats (6, 8). In addition, SHRs have higher tissue catecholamine concentrations (33) and catecholamine-induced myocardial adenyl cyclase activity than normotensive controls (34). These conditions result in increased cyclic adenosine monophosphate formation, predisposing SHRs to decreased glycogen synthase and increased glycogen phosphorylase activities in both myocardium and liver. Furthermore, SHRs are reported to have higher intracellular Ca++ concentrations than normotensive controls (35), which have been shown to reduce the activity of the insulin-stimulated glucose transporter GLUT-4 (36). This would result in a further reduction in glucose uptake and glycogen synthesis in hypertensive animals than in normotensive animals. Whether this elevation in intracellular Ca++ is further exacerbated in females, possibly contributing to the depressed glycogen response compared with males, is unknown.

The age and sex differences in response to dietary manipulation were not related to the magnitude of hypertension in SHRs because mean arterial blood pressures were similar in all groups. Because both supplemented diets derived the same percentage of energy from protein, which was lower than that in the baseline diet, protein intake also could not have accounted for these age and sex differences in female SHRs that were food deprived for 24 h and then refed. The protein contents of all three diets were well above the minimum requirements for this species (37); therefore, any differences would not be expected to affect the indexes studied.

Studying the direct effects of food deprivation and food deprivation followed by refeeding may lead to the development of regimens designed to protect the hypertrophied heart during metabolic stress while improving later recovery. Refeeding food-deprived, hypertensive (hypertrophied), female rats with supplemented diets increased myocardial glycogen to a greater degree than did food deprivation alone and partially replenished liver glycogen. The overall metabolic effects also depended on the source of energy. Despite similar elevations in myocardial glycogen in both female age groups, refeeding the dextrose-supplemented diet resulted in better repletion of liver glycogen in the younger females and a less detrimental effect on serum fatty acid concentrations in the older females than did the oil-supplemented diet.

Conclusion

This study showed that in chronically hypertensive rats there were significant sex differences in baseline fatty acid and liver glycogen concentrations. High fatty acid concentrations, in association with myocardial ischemia, are reported to increase the incidence of arrhythmias and depress pump function (25, 26). Increased serum fatty acid concentrations in females could partially explain the increased morbidity and mortality occurring in female patients with coronary artery disease or hypertrophy. Furthermore, a period of food deprivation followed by refeeding with either a carbohydrate- or lipid-enriched diet can significantly increase the content of myocardial glycogen in both young and older female rats with myocardial hypertrophy. The optimal diet required to augment myocardial glycogen in females has yet to be determined. Diets might be specially formulated to meet the specific needs of individuals. Such diets should prove to be useful clinical adjuncts for patients at risk for ischemic injury, including those requiring medical interventions that produce periods of low coronary perfusion, such as coronary angioplasty. The results of this study showed that there were sex differences in metabolic profiles in response to chronic hypertension and concomitant myocardial hypertrophy. Thus, sex-specific diets are clinically relevant and should be developed as a supplemental method to enhance myocardial protection and improve outcome in female patients.

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