Red Wine and Beer Elevate Blood Pressure in Normotensive Men

Renate R. Zilkens, Valerie Burke, Jonathan M. Hodgson, Anne Barden, Lawrence J. Beilin, Ian B. Puddey

Abstract—A positive relationship between alcohol consumption and blood pressure (BP) is well-established but the relative effect of specific alcoholic beverages is controversial. This study aimed to determine whether red wine may improve vascular function and have less of an impact on blood pressure because of its high content of antioxidant vasodilator polyphenolic compounds. Healthy normotensive men entered a 4-period crossover study comparing in random order 4 weeks of control–abstinence with similar periods of daily consumption of red wine (375 mL; 39 grams alcohol), de-alcoholized red wine (375 mL), or beer (1125 mL; 41 grams alcohol). Ambulatory systolic BP and diastolic BP and heart rate (HR) were measured together with vascular function as assessed by flow-mediated dilatation (FMD) and glyceryl trinitrate-mediated (GTNMD) dilatation of the brachial artery. The systolic and diastolic BP and HR were not different between control–abstinence and de-alcoholized red wine. However, compared with control–abstinence, both red wine and beer increased awake systolic BP (2.9 and 1.9 mm Hg, respectively; P<0.05) and asleep HR (5.0 and 4.4 bpm; P<0.05). There were no specific effects of red wine, de-alcoholized red wine, or beer on FMD or GTNMD. Daily consumption of ~40 grams alcohol as either red wine or beer for 4 weeks results in similar increases in systolic BP and HR. De-alcoholized red wine did not lower BP, and neither red wine nor de-alcoholized red wine influenced vascular function, suggesting that red wine polyphenolics do not have a significant role in mitigating the blood pressure-elevating effects of alcohol in men. (Hypertension. 2005;45:874-879.)

Key Words: alcohol ■ blood pressure ■ endothelin ■ endothelium ■ heart rate ■ human ■ vasodilation

Impairment in flow-mediated dilatation (FMD) of the brachial artery is considered to be an early marker of endothelial function and has been shown to prospectively predict cardiac events. Some human studies have suggested that the acute consumption of red wine may improve FMD, although this observation has not been consistent, possibly as a consequence of simultaneous vascular effects of alcohol. The acute ingestion of de-alcoholized red wine or the short-term administration of purple grape juice to subjects with coronary artery disease have both been associated with improvements in FMD. Although the majority of these observations have been uncontrolled, they have been interpreted as supporting the hypothesis that vasoconstrictor antioxidant polyphenols, found in red wine and purple grape juice, may be beneficial for endothelial function.

Such a hypothesis, however, also has to consider the well-known positive linear relationship between alcohol intake and blood pressure (BP) in regular alcohol drinkers, a relationship that was first documented in 1915 in predominantly wine-consuming French troops serving on the Western front. Intervention studies since have consistently shown a BP-raising effect of alcohol, which is reversible in both normotensive and hypertensive subjects. However, evidence that the type of alcoholic beverage consumed may influence the magnitude of this BP-raising effect comes primarily from cross-sectional epidemiological data with studies from the USA, Norway, France, and Northern Ireland, all suggesting that beer and spirit consumption may be associated with higher BP (particularly systolic) than wine consumption. In the London Civil Servant study, an inverse association between wine and BP was seen, but only in men who drank at least 4 glasses of wine each day.

Patterns of alcohol intake can influence BP. Consequently, comparing episodic beer drinkers with regular daily wine drinkers might obscure the relationship between alcohol intake and BP levels. Furthermore, preference for a beverage type has dietary and several other lifestyle correlates related to BP. Although epidemiological studies have generally adjusted for conventional risk factors such as weight, age, and smoking, these other potential confounders have not been factored into previous analyses, thereby weakening the argument for a specific and independent association of wine intake with lower BP.

Received October 19, 2004; first decision November 16, 2004; revision accepted March 23, 2005. From the School of Medicine and Pharmacology, Royal Perth Hospital Unit, University of Western Australia and the Western Australian Institute for Medical Research, Perth, Western Australia. Correspondence to Dr Renate Zilkens, School of Medicine and Pharmacology, Royal Perth Hospital Unit, Rear 50 Murray Street, GPO Box X2213, Perth WA 6847, Australia. E-mail renaete@cyllene.uwa.edu.au © 2005 American Heart Association, Inc.

Hypertension is available at http://www.hypertensionaha.org DOI: 10.1161/01.HYP.0000164639.83623.76
Animal19 and in vitro studies20–24 also suggest that red wine may modulate vascular function. The vasodilating agents in red wines, grape juices, and grape skin extracts appear to be polyphenolic flavonoids, which are thought to mediate relaxation by nitric oxide mechanisms.22–25 Further in vitro evidence also suggests that red wine polyphenols may inhibit the synthesis of endothelin-1 (ET-1), a potent vasoconstrictor,26 whereas animal data suggest that alcohol can increase ET-1 levels.27–29 Hence, it is difficult to predict what the overall net effect of red wine, which contains both alcohol and polyphenols, might be on ET-1 levels.

Given the epidemiological data and the potentially vasoactive constituents in red wine, the aim of the present study was therefore to determine the relative effects of regular beer consumption compared with red wine or de-alcoholized red wine on both vascular function (FMD) and BP.

Methods

Subjects

Twenty-eight healthy, nonsmoking, male drinkers aged 20 to 65 years with a regular daily alcohol intake between 30 to 60 grams were recruited by advertisement. Exclusion criteria included smoking within the past 6 months, body mass index >30 kg/m², evidence of cardiovascular disease (by clinical history, physical examination), diabetes mellitus, BP >160/90 mm Hg, or treatment with an antihypertensive agent or any medications known to influence endothelial function (eg, aspirin and lipid-lowering agents) or a total cholesterol >7.5 mmol/L. All subjects gave written informed consent. The Human Ethics Committee of the University of Western Australia approved the study protocol.

Study Design

After a 2-week run-in period during which subjects abstained from alcohol, they were randomized using a random number table in combination with a block assignment schedule into a 4-period open-label crossover study. The 4 interventions included: abstention from all alcohol and grape products (control period), 375 mL red wine (Jacobs Creek Shiraz-Cabernet 13% alcohol/vol, 2023 mg/L polyphenols), 375 mL of the same red wine that had been de-alcoholized by Vinpac International and Australian Vintage (South Australia) using spinning cone column technology (0% alcohol/vol, 2044 mg/L polyphenols), and 3 × 375 mL cans Emu Bitter beer (4.6% alcohol/vol, The Swan Brewery Co Pty Ltd) each day for 4 weeks. Red wine was made with grapes destemmed before crushing with an automated noninvasive oscillometric device (Spacelab Aspen 128 ultrasound device; Acuson Corporation) after an overnight fast as previously detailed.30 Glyceryl trinitrate-mediated dilatation was measured to assess endothelium-independent dilatation. The ultrasound scans were analyzed by 2 observers blinded to subject identity and study phase. The coefficient of variation (CV) for repeated within-subject measurement was 19.4% and 15.8% for FMD and glyceryl trinitrate-mediated dilatation, respectively.

Endothelial Function

Endothelial function was assessed twice at the end of each intervention by ultrasound measurement of endothelium-dependent postischemic FMD of the brachial artery using ultrasonography (ACUSON Aspen 128 ultrasound device; Acuson Corporation) after an overnight fast as previously detailed.30 Glyceryl trinitrate-mediated dilatation was measured to assess endothelium-independent dilatation. The ultrasound scans were analyzed by 2 observers blinded to subject identity and study phase. The coefficient of variation (CV) for repeated within-subject measurement was 19.4% and 15.8% for FMD and glyceryl trinitrate-mediated dilatation, respectively.

ET-1

Aliquots of urine from 24-hour urine collections were stored at −80°C until batch-analyzed by radioimmunoassay after extraction using Amprep C2 columns as previously described.31

Assessment of Phenolic Compounds by Gas Chromatography–Mass Spectrometry in Urine

Urinary phenolic acids were measured as previously described, with minor modifications.32 Aliquots from 24-hour urine collections were stored at −80°C until the end of the study. All samples from each subject were assayed in the one batch.

Biochemical Analyses

Blood was collected after an overnight fast. Serum samples were analyzed on the day of venipuncture by Core Laboratory Services, Royal Perth Hospital, using the Hitachi 917 Biochemical Analyser (Hitachi Limited, Tokyo, Japan). The γ-glutamyl transpeptidase was measured with a Roche enzymatic colorimetric kit (catalog number 12016958; Roche Diagnostics GmbH) (interassay CV 1.4%; normal reference range <60 U/L).

Statistics

ABPM data were analyzed using repeated measures models allowing for the correlated error structure in the data (Proc Mixed; Statistical Analysis Program; SAS Institute). The remaining data were analyzed using SPSS 11 statistical software (SPSS) with GLM repeated measures for normally distributed data and was considered significant with Bonferroni correction for multiple comparisons.32 Data not normally distributed were examined with Wilcoxon signed ranks test, with significance set at P = 0.008 for paired comparisons to allow for 6 possible treatment comparisons. Data analyzed with SPSS were tested for period time and treatment order effect with univariate ANOVA. Baseline data are reported as mean ± standard deviation. Nonbaseline values are reported as mean ± standard error except for log-transformed data, which are expressed as geometric mean (95% confidence interval) and non-normal data, which are expressed as median (interquartile range). Analysis was confined to participants who completed the study. The study was powered on the basis of being able to detect an absolute treatment difference in FMD of 2% or larger (80% power, α of 0.0083 to provide for 6 paired comparisons).

Results

Twenty-four of the 28 white men recruited completed the study; 1 man was withdrawn after atrial fibrillation developed, 2 withdrew because of changes in work/family commitments, and 1 withdrew because he could not comply with treatment regimen. They were mainly middle-aged (range, 39 to 65 years; mean, 53 years), slightly overweight (body mass index 25.3 ± 2.6 kg/m²), normotensive, normolipidemic, and regularly consumed 43 ± 10 grams alcohol per day (Table 1). The estimated duration of current drinking habits was 21 ± 11 years. Fifteen had never smoked. The remaining 9 were ex-smokers who had ceased smoking for at least 3 years, with an average consumption of 11 pack-years. Vitamin supplements were ceased 2 weeks before study entry by 3 partici-
pants. Self-report of all alcohol consumed during each study intervention period revealed nonauthorized consumption of alcoholic beverages occurred 7 times. Table 2 details the biomarkers for beverage compliance. Compared with the control–abstinence period, red wine and beer increased \( -\text{GT} \) by 20% and 25%, respectively \( (P < 0.05) \). There was a highly significant 6-fold increase in urinary 4OMGA excretion for red wine and de-alcoholized red wine, whereas beer doubled both 4OMGA and ferulic acid excretion.

The Figure shows the diurnal profiles for systolic BP, heart rate (HR), and beverage consumption on the day of ambulatory BP monitoring. These measures were performed on either the last or the second last day of each intervention. Most of the drinking occurred in the evening between 5:00 PM and 9:00 PM. Table 3 shows the results from 24-hour ABPM and HR monitoring. Compared with control–abstinence, both red wine and beer increased 24-hour systolic BP \( (2.2 \text{ and } 1.7 \text{ mm Hg, respectively; } P < 0.05) \), with most of this effect seen while subjects were awake (Figure and Table 3). The systolic and diastolic BP and HR were not different between control–abstinence and de-alcoholized red wine interventions. Nor were there any differences in these 3 parameters between beer and red wine interventions. Compared with the control–abstinence intervention, both red wine and beer increased HR for 8 to 10 hours after drinking (Figure), increasing asleep HR by 5.0 and 4.4 bpm, respectively \( (P < 0.05) \). There were no specific effects of red wine, de-alcoholized red wine, or beer on FMD and ET-1 (Table 4). However, \textit{post hoc} comparison of the averaged results from the 2 alcohol periods (ie, beer and red wine) and nonalcohol periods (ie, abstinence and de-alcoholized red wine) found that alcohol increased urine ET-1 excretion \( [15.4 \text{ (12.9,18.5) } \text{ versus } 17.5 \text{ (14.4, 21.4) } \text{ ng/d; } P = 0.014] \). There was no

### TABLE 1. Demographic Profile at Baseline (n=24)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>53.3 ± 7.7</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>80.0 ± 9.4</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>25.3 ± 2.6</td>
</tr>
<tr>
<td>Fasting serum lipids, mmol/L</td>
<td></td>
</tr>
<tr>
<td>Total cholesterol</td>
<td>4.90 ± 0.48</td>
</tr>
<tr>
<td>LDL cholesterol</td>
<td>3.21 ± 0.47</td>
</tr>
<tr>
<td>HDL cholesterol</td>
<td>1.28 ± 0.29</td>
</tr>
<tr>
<td>Triglyceride*</td>
<td>0.79 (0.65, 0.96)</td>
</tr>
<tr>
<td>( \gamma \text{-GT}, \text{U/L} )</td>
<td>20.0 ± 4.2</td>
</tr>
</tbody>
</table>

Characteristics were measured at end of the 2-week run-in period. Values are expressed as mean±SD or when indicated (*) geometric mean and 95% CI.

BMI indicates body mass index; CI, confidence interval; \( \gamma \text{-GT}, \) gamma-glutamyl transpeptidase; HDL, high-density lipoprotein; LDL, low-density lipoprotein.

### TABLE 2. Weight and Compliance Biomarkers at End of Each 4-Week Beverage Intervention

<table>
<thead>
<tr>
<th></th>
<th>Abstinence–Control</th>
<th>De-alcoholized Red Wine</th>
<th>Red Wine (39 grams alcohol/day)</th>
<th>Beer (41 grams alcohol/day)</th>
<th>( r \text{ANOVA} )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight, kg</td>
<td>79.59±1.98</td>
<td>79.41±1.92†</td>
<td>80.04±1.89</td>
<td>80.25±1.94</td>
<td>0.005</td>
</tr>
<tr>
<td>( \gamma \text{-GT}, \text{U/L} )</td>
<td>17.7 ± 0.7</td>
<td>18.0 ± 0.7‡</td>
<td>21.3 ± 0.8§</td>
<td>22.2 ± 0.9§</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>4-O-methyl gallic acid, ( \mu \text{g/d}^\ast )</td>
<td>71 (141)</td>
<td>438 (638)§</td>
<td>405 (480)§</td>
<td>142 (287)†§</td>
<td>—</td>
</tr>
<tr>
<td>Ferulic acid, ( \mu \text{g/d}^\ast )</td>
<td>737 (1219)</td>
<td>817 (1251)</td>
<td>999 (1117)</td>
<td>1485 (1743)†§</td>
<td>—</td>
</tr>
</tbody>
</table>

Data represent mean±standard error or, when indicated (*) median (interquartile range).

Significantly different from: †beer, ‡red wine, \( \ast \)abstinence–control.

GLM repeated measures used for weight and plasma \( \gamma \text{-GT}, \) with \textit{post hoc} analysis by modified \( t \) test with Bonferroni correction \( (P < 0.05) \).

Wilcoxon signed ranks test used for urinary polyphenolics with significance set at \( P < 0.008 \).
alcohol effect on FMD (5.89 ± 0.46% versus 5.13 ± 1.13%; P=0.2).

**Discussion**

The present study in healthy, normotensive, moderate-drinking men provides the first evidence to our knowledge from a randomized controlled intervention study that both red wine and beer elevate BP, with no detectable difference in the magnitude of this effect. The vasopressor effect of a daily intake of 4 standard drinks of beer and red wine resulted in respective increases of 1.7 and 2.2 mm Hg in 24-hour systolic BP when compared with 4 weeks of abstinence. In addition, a daily intake of ∼760 mg of polyphenols in de-alcoholized red wine for 4 weeks did not lower 24-hour BP. This study also demonstrated that regular daily consumption of 4 standard drinks of either beer or red wine for periods of 4 weeks does not alter endothelial function as assessed by FMD of the brachial artery. Nor was there any evidence to suggest any beneficial effect of de-alcoholized red wine to improve brachial artery response. The significant increases in the alcohol biomarker, γ-glutamyl transpeptidase, during the alcohol periods, and a concomitant 6-fold increase in the red wine biomarker, 4OMGA, during the wine periods and a 2-fold increase in the beer biomarker, furic acid, during the beer period confirmed subject compliance with the protocol.

The evidence generating the hypotheses that red wine may have less of a BP-raising effect than other alcoholic beverages comes from 4 cross-sectional epidemiological studies. The results from those studies are limited, revealing only possible associations rather than specific evidence for causal relationships. The present study results serve to reject this hypothesis, with red wine (39 grams alcohol/d) increasing BP to similar levels to those seen when alcohol was consumed in the form of beer (41 grams alcohol/d). The magnitude of the change in BP from either beverage was commensurate with that predicted from a recent meta-analysis of all randomized controlled trials of the effects of alcohol reduction on BP. A possible explanation for the different conclusion drawn from this study compared with epidemiological studies is that there may have been inadequate adjustment for confounding diet and lifestyle factors in the population-based studies. Specifically, the associations of a healthier diet and a higher socioeconomic status and hence a better access to health care among wine drinkers, and not the consumption of wine per se, may have been responsible for lower BP in the wine-drinking populations. The present study using ambulatory BP readings confirms that even in normotensive subjects, alcohol from beer and wine has a BP-raising effect, even though red wine is rich in vasodilator phenolic antioxidants. The observation of an increase in urinary ET-1 excretion during either red wine or beer ingestion raises the further possibility that the vasopressor effects of alcohol were caused, at least in part, via alcohol-induced increase in ET-1, and do not support the contention from in vitro data that red wine will inhibit ET-1 synthesis.

**TABLE 3. Results from 24-Hour Ambulatory Blood Pressure Monitoring Conducted at the End of Each 4-Week Beverage Intervention**

<table>
<thead>
<tr>
<th>Blood Pressure</th>
<th>Abstinence Control</th>
<th>De-alcoholized Red Wine</th>
<th>Red Wine</th>
<th>Beer</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>24-hour SBP</td>
<td>122.8±0.48</td>
<td>123.5±0.48*</td>
<td>125.0±0.48‡</td>
<td>124.5±0.48‡</td>
<td>0.0047</td>
</tr>
<tr>
<td>Awake SBP</td>
<td>126.6±0.79</td>
<td>127.4±0.78*</td>
<td>129.5±0.79‡</td>
<td>128.5±0.79‡</td>
<td>0.0018</td>
</tr>
<tr>
<td>Asleep SBP</td>
<td>109.8±1.46</td>
<td>109.8±1.43</td>
<td>110.7±1.42</td>
<td>110.8±1.46</td>
<td>NS</td>
</tr>
<tr>
<td>24-hour DBP</td>
<td>77.0±0.38</td>
<td>77.1±0.38</td>
<td>77.9±0.38</td>
<td>77.7±0.38</td>
<td>NS</td>
</tr>
<tr>
<td>Awake DBP</td>
<td>80.0±0.63</td>
<td>80.1±0.61*</td>
<td>81.4±0.62‡</td>
<td>80.9±0.62</td>
<td>0.066</td>
</tr>
<tr>
<td>Asleep DBP</td>
<td>66.2±1.11</td>
<td>65.5±1.08</td>
<td>65.8±1.07</td>
<td>66.1±1.10</td>
<td>NS</td>
</tr>
</tbody>
</table>

**TABLE 4. Results From Vascular Studies at the End of Each 4-Week Beverage Intervention**

<table>
<thead>
<tr>
<th>Vascular Function</th>
<th>Abstinence Control</th>
<th>De-alcoholized Red Wine</th>
<th>Red Wine</th>
<th>Beer</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>FMD</td>
<td>6.09±0.43</td>
<td>5.71±0.52</td>
<td>6.50±0.63</td>
<td>6.38±0.66</td>
<td>0.29</td>
</tr>
<tr>
<td>GTNMD</td>
<td>20.1±1.0</td>
<td>20.6±1.2</td>
<td>21.2±1.3</td>
<td>21.2±1.1</td>
<td>0.23</td>
</tr>
<tr>
<td>Endothelin-1 (*)</td>
<td>14.5 (11.2, 18.9)</td>
<td>14.7 (12.0, 18.2)</td>
<td>18.0 (14.3, 22.8)</td>
<td>16.0 (12.9, 19.9)</td>
<td>0.21</td>
</tr>
</tbody>
</table>

Data are mean±standard error or when indicated (*) geometric mean and 95% CI.

DBP indicates diastolic blood pressure (mm Hg); HR, heart rate (bpm); NS, not significant; SBP, systolic blood pressure.

Significantly different from: *red wine, †beer, ‡abstinence–control.

Endothelin-1 is 24-hour urine excretion of endothelin-1 (ng/day).
The current study supports previous findings of increases in HR with increases in alcohol intake. In both hypertensive and normotensive men, the effect of alcohol to increase HR have been more pronounced during the evening and night. The dissociation between changes in BP and HR with systolic BP increasing during the day and HR increasing at night in our study support previous findings and are consistent with diurnal differences in the effects of alcohol on sympathovagal balance. We did not study ET-1 levels in relation to diurnal differences in BP and HR. Such studies could help clarify the relationship between ET-1 levels and sympathovagal balance.

To our knowledge, this is the first controlled short-term beverage intervention study that has studied the effect of beer, red wine, and de-alcoholized red wine on endothelial function as assessed by FMD of the brachial artery. However, there have been 2 uncontrolled studies that reported that short-term ingestion of purple grape juice (4 to 8 mL/kg per day for 2 to 4 weeks) improves endothelial function (FMD) in adults with coronary artery disease. Both these studies were interpreted as evidence for improved endothelium-dependent vasodilatation secondary to the antioxidant flavonoids found in grape juice. Unfortunately, however, these studies were neither randomized nor did they have a control beverage group with low flavonoid content for comparison. In addition, in both studies the grape juice was consumed on the morning of the assessment of endothelial function, thus making it difficult to ascertain whether the improvement was a result of “acute” or “short-term” intake. These shortcomings make it difficult to compare those published results with our finding that de-alcoholized red wine does not improve FMD. Because our study was well-controlled, the evidence for a lack of effect of red wine polyphenols to improve endothelium-dependent vasodilation secondary to antioxidant flavonoids carries greater weight than the grape juice trials. However, the “healthy drinker” status of our study subjects may have contributed to the lack of a detectable change in endothelial function after any, or all, treatment interventions (ie, red wine, beer, or de-alcoholized red wine).

**Perspectives**

The results of the present study suggest that in healthy normotensive men, daily consumption of 40 grams of alcohol as either red wine or beer for 4 weeks results in similar increases in both 24-hour systolic BP and HR, with the predominant BP-raising effect seen during the day and a predominant acceleration of HR occurring at night, immediately after ingestion of alcohol. It appears likely that the ability of alcohol beverages to raise BP is caused by the alcohol. The study did not detect any significant effect of beverage type on endothelial function and de-alcoholized red wine did not lower BP compared with abstinence, so it is unlikely that in predominantly normotensive men red wine polyphenolics have any significant role in lowering BP and do not mitigate against the BP-elevating effects of alcohol.

**Acknowledgments**

This study was supported by grant 981707 from the National Health and Medical Research Council of Australia.

**References**


13. Bulsitt CJ, Shipley MJ, Demmen A. The contribution of a moderate “healthy drinker” status of our study subjects may have contributed to the lack of a detectable change in endothelial function after any, or all, treatment interventions (ie, red wine, beer, or de-alcoholized red wine).


31. Zilkens et al Red Wine and Beer Elevate BP in Men 879


Red Wine and Beer Elevate Blood Pressure in Normotensive Men
Renate R. Zilkens, Valerie Burke, Jonathan M. Hodgson, Anne Barden, Lawrence J. Beilin and Ian B. Puddey

Hypertension. 2005;45:874-879; originally published online April 18, 2005;
doi: 10.1161/01.HYP.0000164639.83623.76
Hypertension is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2005 American Heart Association, Inc. All rights reserved.
Print ISSN: 0194-911X. Online ISSN: 1524-4563

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://hyper.ahajournals.org/content/45/5/874

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Hypertension can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Hypertension is online at:
http://hyper.ahajournals.org/subscriptions/