Original Article

Comparison of the Effects of Alcoholic and Non-Alcoholic Red Wine on Flow-Mediated Dilation and Brachial Artery Vasodilation

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Abstract

Background: **Cardiovascular diseases are the leading cause of mortality worldwide. Wine consumption has been associated with cardiovascular benefits, which are attributed to the presence of flavonoids.**

Objectives: **To assess the effects of alcoholic and non-alcoholic red wine on endothelial function by measuring variations in brachial artery flow-mediated dilation (FMD) and analyzing changes in arterial diameter, heart rate, and blood pressure.**

Methods: **A randomized, parallel, controlled clinical trial was conducted with 22 participants assessed at 2 distinct time points. Participants consumed 200 mL of red wine and, after a 7-day washout period, received 200 mL of non-alcoholic wine. Data were analyzed using Student's t test. P values < 0.05 were considered statistically significant.**

Results: **Pre-ischemia brachial artery diameter increased after both interventions: with alcoholic wine (3.21 ± 0.46 mm before versus 3.51 ± 0.53 mm after; p < 0.001) and non-alcoholic wine (3.16 ± 0.48 mm before versus 3.31 ± 0.58 mm after; p = 0.003). FMD showed a decrease after consumption of alcoholic wine (11.88% ± 8.40% before versus 5.98% ± 5.34% after; p = 0.007), whereas consumption of non-alcoholic wine did not result in significant changes (7.26% ± 6.39% before versus 6.01% ± 5.85% after; p = 0.572). Other parameters, such as heart rate and blood pressure, did not show any significant differences.**

Conclusion: **Consumption of red wine, with and without alcohol, increased brachial artery diameter. However, alcoholic red wine was associated with reduced FMD, suggesting that ethanol may negatively affect endothelial function.**

Keywords: **Vasodilation; Wine; Resveratrol; Flavonoids; Endothelium; Cardiovascular Diseases.**

Introduction

Endothelial function plays an important role in cardiovascular health, as it is responsible for maintaining physiological vasodilation by nitric oxide as well as anti-inflammatory and antioxidant mechanisms. Endothelial dysfunction actively contributes to the pathogenesis of atherosclerosis, facilitating the oxidation of low density lipoprotein (LDL) cholesterol and platelet adhesion, increasing the risk of cardiovascular disease, which is the leading cause of death worldwide.[1-3]

Although medical treatments are indispensable in cardiovascular disease, it is essential to consider non-pharmacological interventions. For example, lifestyle changes, such as a healthy diet, regular exercise, and abstinence from tobacco are fundamental to the prevention and treatment of these diseases.[4]

In spite of the risks of alcohol abuse, some data have suggested that moderate consumption (especially of wine) may offer a cardioprotective effect.[5-8] Studies have shown that both wine and other alcoholic beverages reduce oxidative stress; however, only wine has shown improved microvascular endothelial dysfunction. This suggests that, in addition to ethanol, other components of wine play an antioxidant role, minimizing endothelial dysfunction.[9,10] The polyphenolic compounds present in wine, such as resveratrol, would act on the endothelium by increasing the release of nitric oxide by endothelial cells.[10,11] These actions on endothelial function could be part of epidemiological findings, such as the well-known "French paradox," which suggests a potential association between a lower incidence of cardiovascular diseases in France and daily consumption of 1 to 2 glasses of wine.[12]

There are still doubts as to whether the positive effects of red wine are associated with alcohol or other components such as resveratrol, which can also be found in dealcoholized wines. Unlike grape juice, non-alcoholic wine undergoes a fermentation process before the alcohol is removed, which can be done by methods such as evaporation, distillation,

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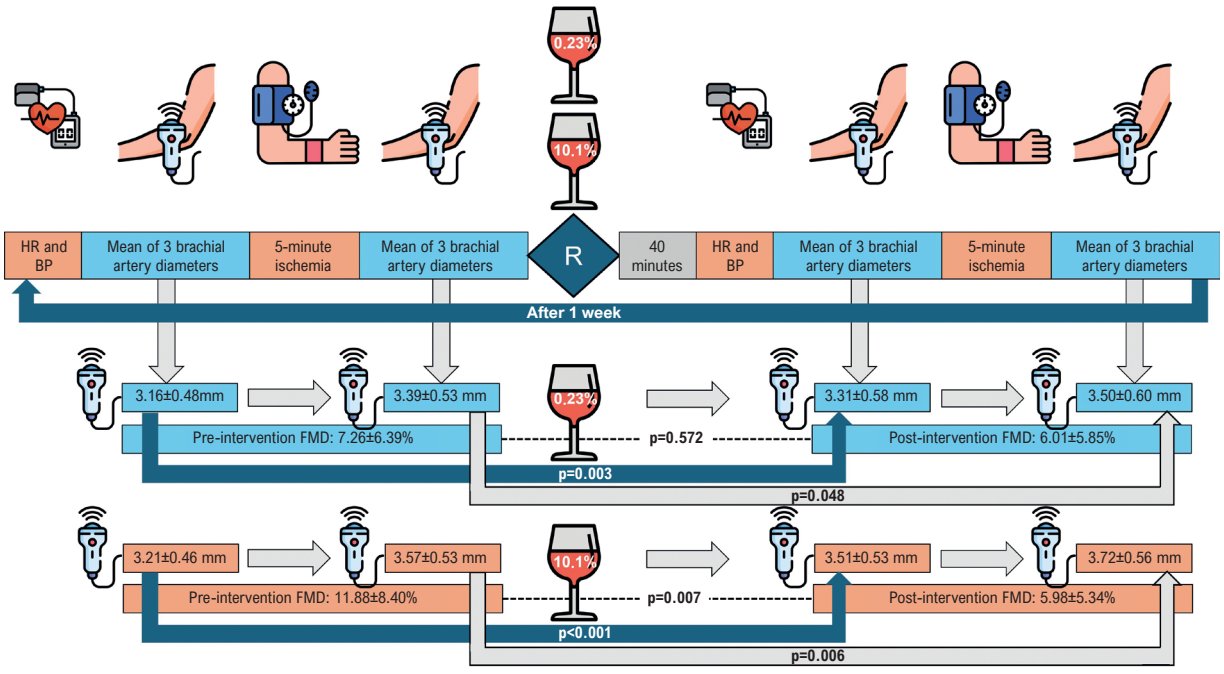
Central Illustration: Comparison of the Effects of Alcoholic and Non-Alcoholic Red Wine on Flow-Mediated Dilation and Brachial Artery Vasodilation



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pervaporation, reverse osmosis, or membrane-based and concentration techniques such as dialysis and osmotic distillation.[13] Given this gap, this study sought to evaluate whether alcoholic red wine has acute effects on endothelial function in presumably healthy individuals, in comparison with non-alcoholic wine.

Methods

This is a randomized, parallel, controlled clinical trial with a blinded assessor, in which volunteers were selected to consume alcoholic red wine and, at another time point, non-alcoholic wine, in an academic environment.

The main outcome was the comparison of flow-mediated vasodilation (FMD) after consumption of alcoholic and non-alcoholic red wine. The secondary outcomes were changes in brachial artery diameter (in mm) at rest and after brachial ischemia, heart rate (in bpm), and blood pressure.

The inclusion criteria were age between 18 and 40 years and occasional alcohol consumption. The exclusion criteria were individuals using medications with cardiovascular effects, such as antihypertensives, including beta-blockers and calcium channel blockers; alcohol abuse; and pregnancy or possible pregnancy.

A sample of 44 cases (22 pairs) was determined to detect a difference of 0.11% in changes in pre- and post-intervention brachial artery FMD with red wine, at a 2-tailed alpha of 0.05 and power of 80%, estimating a loss of 10%, based on data from the study by Colombo et al.[14]

Randomization was performed using specific software (Sealed Envelope ™)[15] into 2 groups in blocks of 4. Random allocation was maintained by a randomization sequence prepared by an independent researcher, which was only opened after the free and informed consent form was signed and the collection form was filled out. Considering a concentration of approximately 0.8 mg/mL of flavonoids in wines produced with Bordeaux grapes,[16] 2 groups were formed. The alcoholic wine group received 200 ml of red wine containing an estimated 150 mg of flavonoids ("La Dorni" demi-sec Bordeaux, 10.1% alcohol at 20 ºC, produced by Alves & Martins Especiais LTDA, Bandeirantes, Paraná, Brazil). The control group received 200 ml of non-alcoholic wine containing approximately 150 mg of flavonoids ("Casa Navaronne" demi-sec Bordeaux, 0.23% alcohol at 20 ºC, produced by Alves & Martins Bebidas Especiais LTDA, Bandeirantes, Paraná, Brazil).

All participants involved were asked at rest for 30 minutes before the initial assessment in order to minimize external impacts on endothelial function. In addition to brachial artery diameter, blood pressure and heart rate were also measured.

After measuring heart rate and blood pressure, ultrasound assessments were performed at 2 distinct time points: 3 measurements before brachial ischemia, calculating their average, and another 3 measurements after brachial

Table 1 – Participant profile

Characteristics	
Age (years), mean ± SD	24.86 ± 3.28
Men, n (%)	5.00 (22.72)
Weight (kg), mean ± SD	61.27 ± 10.07
BMI (kg/m^2), mean ± SD	22.05 ± 2.22
Regular physical activity, n (%)	18.00 (81.80)
Average weekly physical activity (min), mean ± SD	186.40 ± 117.40
Prior consumption of wine, n (%)	18.00 (81.80)
Smoking, n (%)	2.00 (9.09)

BMI: body mass index; SD: standard deviation.

ischemia. Brachial ischemia was promoted by inflating the cuff to suprasystolic pressure values: 50 mmHg above the systolic blood pressure value for 5 minutes. Subsequently, the intervention was performed, in which each participant ingested 200 ml of the beverage selected according to randomization; 40 minutes later, they were evaluated by the same trained and blinded assessor. Heart rate and blood pressure measurements were taken, followed by 2 ultrasound assessments after the intervention, performed in the same manner (3 measurements before brachial ischemia, calculating their average, and another 3 measurements after brachial ischemia). The methods used for data collection were based on the most recent guideline for noninvasive assessment of endothelial function,[3] and ultrasound assessment was always performed on the patient's left brachial artery, using an Invictus C7 Alfamed device. FMD is shown as a percentage and is obtained by dividing the difference between the arterial diameter after ischemia and the initial baseline diameter (Ddiff) by the initial baseline diameter of the artery (Dbase), multiplied by 100.[17] One week after the initial assessment, the groups were crossed; in the second phase of the study, the participants who received alcoholic red wine received non-alcoholic wine and vice versa, and the procedures performed during the previous week were repeated. The Central Illustration displays a schematic representation of the procedures performed.

This study was conducted in accordance with resolutions number 466/2012 and 510/2016 of the Brazilian National Health Council after receiving approval from the Research Ethics Committee. All participants were fully informed regarding the research objectives and procedures, ensuring their anonymity and confidentiality of information. After receiving detailed explanations about the study, all participants read, understood, and signed the free and informed consent form.

Statistical analysis

Data were tabulated and analyzed using SPSS 13.0 software for Windows. The Kolmogorov-Smirnov test was used to verify normal distribution of continuous variables, which were expressed as mean ± standard deviation. We used Student's paired t test for comparisons within the same group and Student's independent t test for comparisons between groups. Categorical variables were expressed as absolute numbers and percentages. P values < 0.05 were considered statistically significant.

Results

This study assessed 22 volunteers, with an average age of 24.86 ± 3.28 years, during the period from August 6 to August 22, 2024. Table 1 displays the other characteristics of the study population.

Both alcoholic and non-alcoholic wine demonstrated a significant increase in the pre-ischemia dilation of brachial artery diameter. Similarly, there was an increase after ischemia in both the alcoholic and non-alcoholic wine groups (Figure 1). There was a decrease in FMD after consumption of alcoholic wine, which did not occur in the non-alcoholic wine group. However, the post-intervention FMD values did not differ between the alcoholic and non-alcoholic wine groups (Figure 2).

Heart rate decreased in patients who received non-alcoholic wine (Table 2). Other results are displayed in Table 2.

None of the participants reported adverse effects.

Discussion

This clinical study has demonstrated that both alcoholic and dealcoholized red wine have significant vasoactive effects that are capable of increasing brachial artery diameter. However, no significant differences were observed in FMD between the two interventions, despite the reduction in FMD after consumption of alcoholic wine.

The vasoactive effect of alcoholic and non-alcoholic wines found in this study and demonstrated by the significant increase in brachial artery diameter could be attributed to the effect of resveratrol. Resveratrol, in turn, stimulates the expression of the enzyme endothelial nitric oxide synthase and promotes the release of nitric oxide, triggering the entry of Ca^{2+} into endothelial cells and subsequent vasodilation.[7,11,18] The vasodilatory effect of alcoholic and non-alcoholic wines has already been proven in animal models.[19] In humans, there are data that have demonstrated the vasodilatory effects of wine regardless of the presence of alcohol.[20]

The vasodilatory effect of dealcoholized wine on the brachial artery, however, does not appear to be consistent and demonstrates that, in addition to stimulation of endothelial nitric oxide synthase, there may be other pathways that promote vasodilation associated with alcohol, for example, its effect in the central nervous system on vascular tone.[19,21,22] The vasodilatory effects of dealcoholized wine, in turn, could be dependent on the specific amount of resveratrol in the wine and the vintage evaluated.

In spite of the proven vasoactive effects, analysis of changes in FMD before and after the interventions demonstrated that alcoholic wine promoted a significant reduction in FMD, an effect that was not observed with

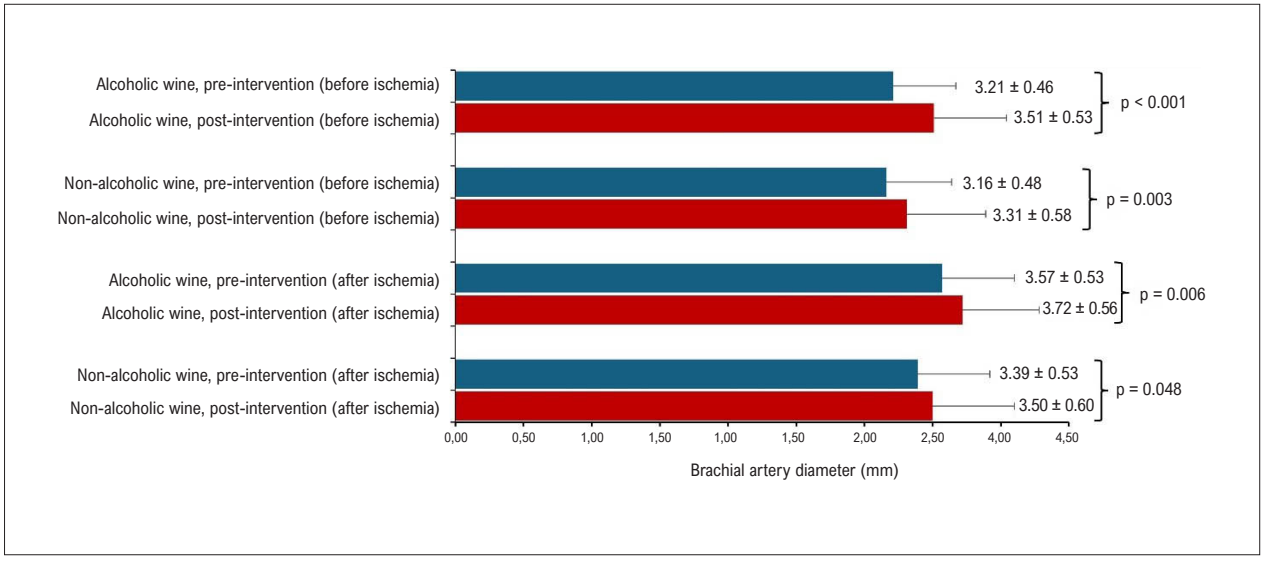

Figure 1 – *Comparison of brachial artery diameter measurements*

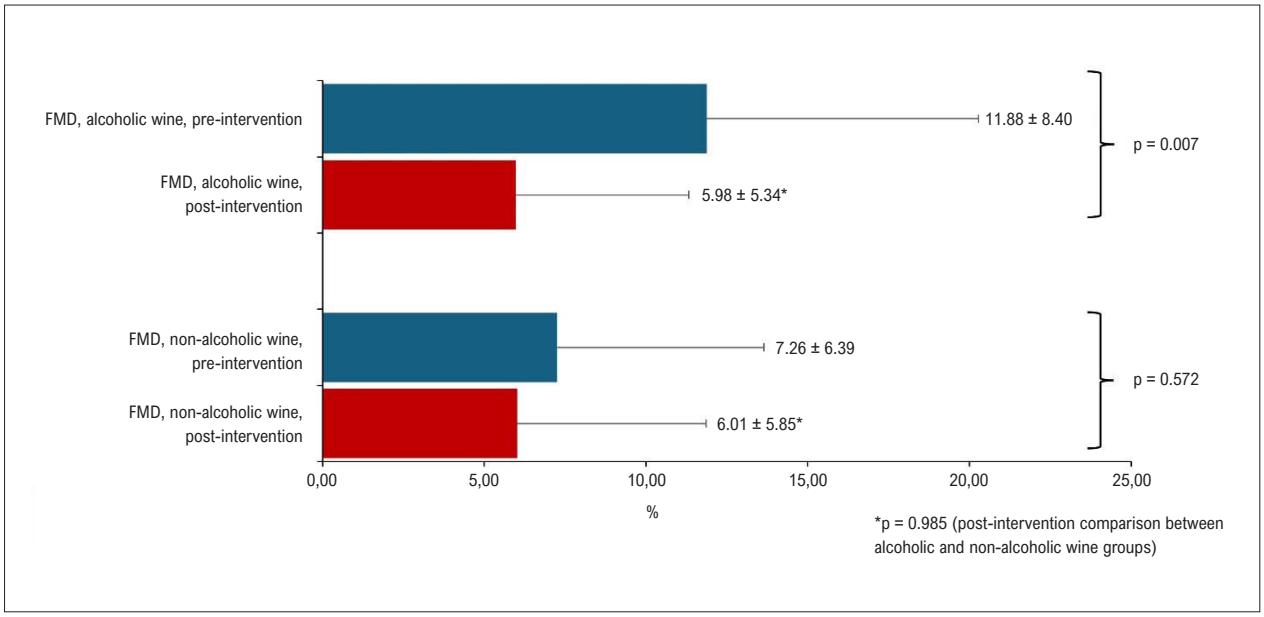

Figure 2 – *Comparison of FMD measurements. FMD: flow-mediated vasodilation.*

Table 2 – Comparison of pre- and post-intervention vital signs

Measurement	Pre-intervention	Post-intervention	p
SBP, alcoholic wine (mmHg)	120.07 ± 14.29	118.34 ± 12.84	0.404
DBP, alcoholic wine (mmHg)	81.29 ± 9.02	81.70 ± 8.09	0.964
SBP, non-alcoholic wine (mmHg)	120.25 ± 14.38	120.32 ± 13.63	0.773
DBP, non-alcoholic wine (mmHg)	80.14 ± 7.09	82.14 ± 8.57	0.131
HR, alcoholic wine (bpm)	80.86 ± 10.32	81.04 ± 10.19	0.920
HR, non-alcoholic wine (bpm)	82.59 ± 11.66	78.90 ± 9.42	0.046

Values shown as mean ± standard deviation. DBP: diastolic blood pressure; HR: heart rate; SBP: systolic blood pressure.

dealcoholized wine. Pragmatically, these findings suggest that, in an acute form, non-alcoholic wine would not have significant effects on endothelial function, whereas alcoholic wine would worsen it.[23] One of the justifications for the reduction in FMD with the consumption of alcoholic wine is a possible inverse relationship between greater resting vessel diameter and FMD, as observed in a similar study.[21] It is, however, worth considering that prior studies have not demonstrated consistent changes in FMD with wine consumption, suggesting that alcohol alone may have neutral or even negative effects on some endothelial functions, for example, increased endothelin-1 expression. On the other hand, antioxidant components present in red wine, such as polyphenols, could improve endothelial function, including FMD.[18,24-26] Furthermore, there is evidence questioning the possibility that wine polyphenols, in an acute form, could act on endothelial function, given that their absorption is low. Thus, the maximum concentrations after ingestion would be insufficient to increase FMD in the case of dealcoholized wine or to "compensate" for the decrease in FMD caused by alcohol, which occurred in this study.[27]

This study's hemodynamic assessments demonstrated that wine did not have an effect on blood pressure, and heart rate reduced with consumption of dealcoholized wine. Data on blood pressure are controversial. Previous studies have suggested that alcoholic wine would have no effect on blood pressure, whereas non-alcoholic wine could reduce it.[18,28] Ambulatory blood pressure monitoring data, in turn, demonstrated a biphasic effect on BP; drinking 230 to 300 ml of red wine (with or without alcohol) during dinner reduced blood pressure during the night, but increased blood pressure during the waking period the following day.[29] Regarding heart rate, data have shown that alcoholic wine can increase heart rate in a dose-dependent manner, whereas non-alcoholic wine does not appear to have a significant effect on heart rate.[18,29] Accordingly, although the results found for blood pressure are supported by previous data, the findings on heart rate do not appear to have a justification and could be merely the result of chance.

This study has some limitations that need to be mentioned. Although the sample was meticulously calculated, it is a small study, and the lack of response in FMD may be due to lack of power. Variations in room temperature (15 to 25 °C) during data collection were not rigorously controlled, which may have influenced the results. The sample was predominantly composed of healthy young women with low cardiovascular risk, thus limiting the generalization of the results. The quantity of flavonoids in the wine was not measured, but rather estimated based on literature data. The characteristics of the wine used, such as the grape variety (Bordeaux) and the terroir of the northern region of Paraná, may have influenced the outcomes, limiting the conclusions to this specific type of wine.

Conclusion

Acute consumption of red wine, with and without alcohol, promoted arterial vasodilation in presumably healthy individuals. FMD did not show significant differences between the two intervention types, but there was a reduction in FMD with alcoholic wine. Heart rate decreased significantly in the group that consumed dealcoholized wine, whereas blood pressure remained unchanged.

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Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

Sources of Funding

There were no external funding sources for this study.

Study Association

This study is not associated with any thesis or dissertation work.

Ethics Approval and Consent to Participate

This study was approved by the Ethics Committee of the Universidade do Sul de Santa Catarina under the protocol number 78483823.4.0000.0261. All the procedures in this study were in accordance with the 1975 Helsinki Declaration, updated in 2013. Informed consent was obtained from all participants included in the study.

Use of Artificial Intelligence

During the preparation of this work, the author(s) used Chat GPT for correcting grammar and punctuation. After using this tool/service, the author(s) reviewed and edited the content as needed and take full responsibility for the content of the published article.

Availability of Research Data

All datasets supporting the results of this study are available upon request from the corresponding author.

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