

## Chapter 55

### The Impact of Juice Plus+® on Early PAD: A Clinical Study

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#### Abstract

This paper involves a retrospective study of patients taking anti-platelet agents alone or in combination with a whole food phytonutrient supplement over 13-48 months. Physiologic lower extremity Doppler studies either remained unchanged or worsened in 17 out of 18 in the anti-platelet-only group. Doppler studies returned to normal in 7 out of 13 in the nutritional supplement group and remained unchanged in the remaining 6. The addition of phytonutrient support to anti-platelet therapy resulted in a significant improvement in post-treatment physiologic Doppler study findings as compared to anti-platelet intervention alone.

#### Introduction

Limb pain can be caused by many conditions and co-morbidity may make the diagnoses of peripheral arterial disease (PAD) at any stage difficult. PAD occurs when blood flow is insufficient to meet the physiologic demands of the limbs either at rest or with exercise. As the disease progresses, claudication — a painful ache, tightness or cramp in the leg muscles that is caused by walking and relieved by rest — can occur [1].

Even without confounding co-morbid factors, PAD remains under-diagnosed. When evaluating a patient for PAD, an index of suspicion, followed by a pertinent history and physical examination, is required. Even in the absence of obvious physical findings, when risk factors are present and the clinical condition is consistent with the diagnosis, ankle-brachial index (ABI) measurements

and vascular Doppler studies are a natural extension of the physical exam [2].

The ABI has been shown to correlate well with exercise level or walking distance. It is not as reliable in patients with long-standing diabetes or atherosclerosis when vessel wall incompressibility due to calcifications is present. Volume flow studies and exercise stress examinations can offer substantial information to complement the information obtained from ABI measurement [3].

PAD is well known to be a marker for systemic atherosclerosis. Furthermore, the severity of oxidative metabolism has an impact both on the resulting symptoms and the progression of disease. As with many disorders, early detection and disease management is favorable as compared to intervention at advanced stages. Treatment begins with patient education concerning both the disease process and risk factor modification [4].

While smoking cessation, controlling blood pressure, blood lipid and sugar levels, exercise and diet modifications are all important, compliance is often a problem at any stage of disease. Using a whole food phytonutrient supplement to increase fruit and vegetable intake offers an appealing option that can increase compliance with healthy diet recommendations.

## Methods and Materials

A retrospective computer search to find out which patients within our practice had undergone two sets of physiologic vascular Doppler studies was performed. We tend to see early arterial disease in combination with neuro-musculoskeletal problems creating co-morbid factors that contribute to pain. In our population, the only reason to perform a second study is to determine if anti-platelet agents that had previously been started can now be discontinued.

An IMEX vascular Doppler lab was used. In all cases, ABI measurements, segmental tests with bi-directional Doppler, and post-exercise Doppler studies were obtained. Pre- and post-treatment findings were compared and classified as improved, equivocal (unchanged) or worsened. Patients were not randomized or controlled for co-morbidities, age or gender. All patients were

counseled about the risk factors involved with PAD at the time of initial diagnosis.

Depending on the clinical situation, everyone was started on either Cilostazol or Clopidogrel. They were also offered the opportunity to begin Juice Plus+®, a phytonutrient product consisting of a blend of fruit (apple, orange, pineapple, cranberry, peach, acerola cherry, papaya) and vegetable (carrot, parsley, beet, kale, broccoli, cabbage, spinach, tomato) juice concentrate that also includes oat and barley bran, taken in a combination of four capsules daily.

## Results

A total of 31 patients were identified. The average interval between studies was 22 months (with the range from 13-48 months). All patients were taking an anti-platelet agent (9 were on Cilostazol and 22 were on Clopidogrel). Thirteen were also taking Juice Plus+®. Of the 18 taking only the anti-platelet agent, 9 showed worsening of their physiologic Doppler studies, 7 were equivocal and 1 was improved. Of the 13 that were also taking Juice Plus+®, 6 showed an improvement in their physiologic Doppler studies and 7 were equivocal. There were 8 males and 6 females in the supplement group and 8 males and 9 females in the anti-platelet-only group. All patients had identifiable risk factors for PAD. The number of patients in the supplement group was 13 and in the anti-platelet group was 18. Their make-up by risk factor included smokers: 3 vs. 5, diabetes: 1 vs. 3, hyperlipidemia: 10 vs. 12, hypertension: 6 each, and prior history of coronary artery disease: 2 each.

All patients with diabetes or hypertension were receiving medical management for their conditions. In the supplement group, 100 percent was either on a statin or diet management for hyperlipidemia vs. 92 percent for the anti-platelet group. Statin usage included 7 of 10 in the supplement group and 6 of 12 in the anti-platelet group.

Of the patients who were improved in the supplement group, 2 of 6 were smokers, 3 of 6 had a prior history of coronary artery disease or hypertension, and 4 of 6 had hyperlipidemia. Of those with hyperlipidemia, 2 were on a statin and 2 were diet controlled. There were no diabetics in the supplement group.

Both the supplement and anti-platelet groups had mild peripheral vascular disease. None of the ABI measurements were below 0.71. All patients received counseling in the benefits of exercise at the time their PAD was diagnosed. Each patient had a combination of early functional claudication and other neuro-musculoskeletal disorder that contributed to their leg pain at the onset of treatment. All were symptomatically improved at the time of their second vascular Doppler study.

The most pronounced improvements occurred in stress studies (converting from abnormal or flat line to flat line or normal). Distal segmental pulse volume improvements were seen as well. Only minor changes were seen in ABI measurements in either group.

### Discussion

There have been several studies showing the health benefits of a diet rich in fruits and vegetables. There are also several studies showing the effectiveness of nutritional support on physiologic parameters. Two prior studies on Juice Plus+® have demonstrated improvement in volumetric blood flow and reduction of plaque formation [5,6].

While the numbers are small, and the study was not blinded, the findings in this study suggest that 41% of patients with early or mild peripheral arterial disease taking Juice Plus+® in combination with an anti-platelet agent showed an improvement in their vascular Doppler stud-

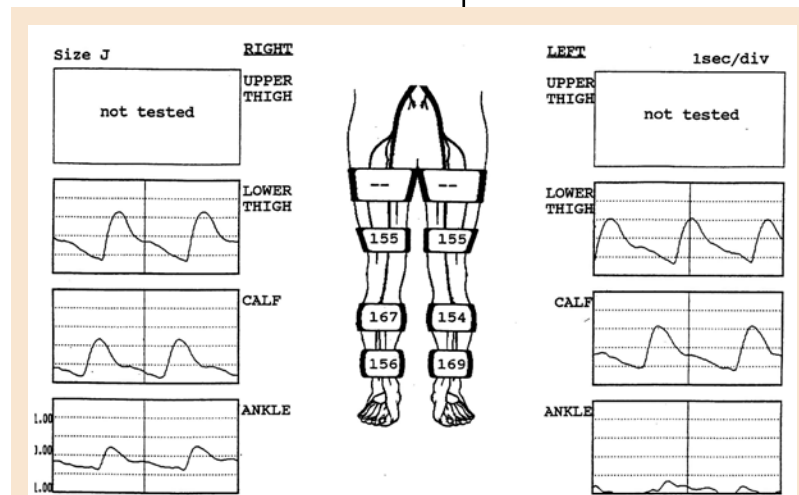
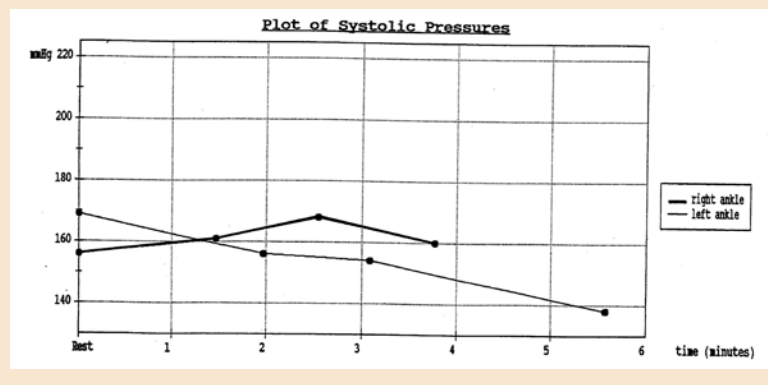


Fig. 1A. Note the decreased pulse volume in the left ankle (bottom, right graph)

Fig. 1B. Note the declining left lower extremity post-exercise systolic pressure graph (below)



ies over an average of 22 months. This is compared to 5.5% in the anti-platelet-only group.

Although the clinical course of PAD is variable, it is generally one of gradual worsening. Disease progression may undergo periods of stabilization, with improvement occurring in up to one quarter and worsening in another quarter of patients [7]. As atherosclerotic changes advance, ischemic pain and related disease can occur. Numbness, paresthesias, and muscle weakness can ensue [8].

Only a minority of PAD patients report classic intermittent claudication. Some accommodate to ischemic symptoms by becoming less active, often without recognizing that they have done so

[9]. The rate of progression is significantly influenced by the extent of existing occlusion, the presence of co-morbid conditions such as diabetes, and whether or not the individual smokes [10].

Early risk factor modification, including dietary changes to low fat food choices, is known to improve the health status of claudicants [11,12]. Optimal management requires lifelong lifestyle changes. The overall therapeutic goals are to reduce risk factors and relieve the symptoms of intermittent claudication, lessen disability and improve functional capacity, prevent gangrene development and limb loss, and avert cardiovascular and cerebrovascular events [13].

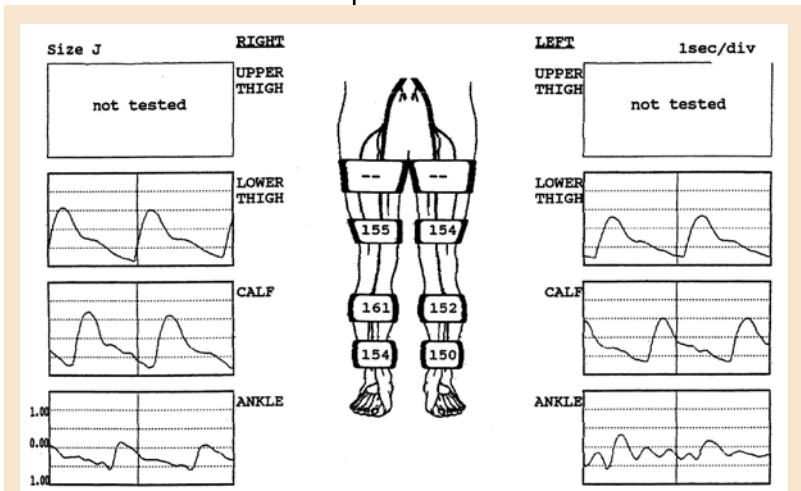
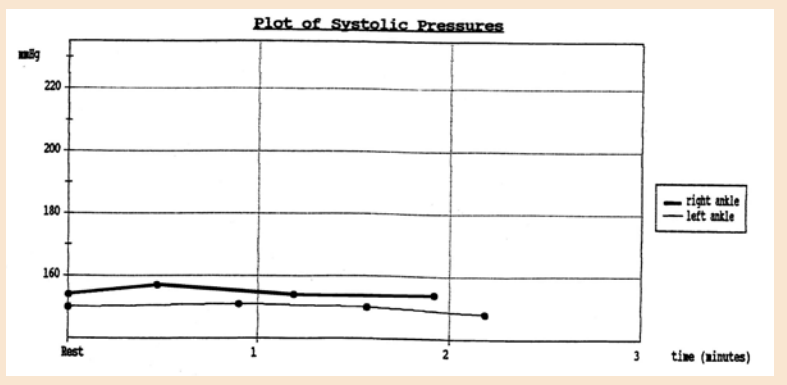


Fig. 2A. Note the improved left ankle pulse volume (bottom, right graph)

Fig. 2B. Note the improved left lower extremity post-exercise systolic pressure graph (below)



## Conclusion

In this uncontrolled, retrospective study, patients with mild PAD who took Juice Plus+®, in addition to Cilostazol or Clopidogrel, showed significantly greater improvement in physiologic stress-Doppler studies after an average of 22 months of treatment than those who took either Cilostazol or Clopidogrel alone.

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