Evaluation of Walking Capacity Over Time in 500 Patients With Intermittent Claudication Who Underwent Clinical Treatment

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Background: The use of physical training in the treatment of intermittent claudication is well established. However, current data do not provide enough information about the prognosis for each case, and there are no data on how walking distances evolve over time with conservative treatment. The goal of this study was to evaluate improvement in walking capacity among patients with intermittent claudication who underwent unsupervised clinical treatment, observing whether sustained treatment would increase or decrease maximum walking distance, whether after 6 months there was a change in the maximum distance, and whether abstinence from smoking and well-conducted walking exercise had independent effects on the outcome.

Methods: Five hundred patients with intermittent claudication were surveyed in a prospective, nonrandomized, and uncontrolled study. Maximum walking distance and treatment compliance over time were analyzed.

Results: Nonsmoking patients who walked achieved a mean increase during the first 6 months of 33.70 m/mo and a mean increase thereafter of 4.24 m/mo. Smokers who walked achieved an increase during the first 6 months only (mean, 42.92 m/mo). Patients who did not practice physical training exhibited no effect (smokers) or negligible effect (nonsmokers) from the treatment (mean, 7.58 m/mo).

Conclusions: Patients who adhered to physical training exhibited a significant increase in maximum walking distance during the first 6 months of treatment only. Patients who did not practice physical training exhibited no effect (smokers) or negligible effect (ex-smokers) from the treatment.

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Division of Vascular Surgery, Hospital das Clínicas, University of São Paulo, were surveyed. This was a prospective, non-randomized, and uncontrolled study. All patients underwent similar treatment, following the same protocol, in accordance with the ethical standards of the university’s Committee of Ethics for Analysis of Research Projects on Human Experimentation and with the Helsinki Declaration of 1975, as revised in 1983.

At the first visit, the extent of arterial occlusion was determined by physical examination (palpation of arterial pulses) and confirmed by duplex scan (model SSH140A; Toshiba Corp, Shibaura, Japan) with transducers of 3.5, 5.0, and 7.5 MHz. All patients had an ankle-brachial index of less than 0.8, assessed by Doppler ultrasound (model 1050-C; Vascular Mini-Lab; Parks Medical Electronics Inc, Aloha, Ore). Many patients (40%) presented with obstruction in the femoropopliteal territory—29.5% in the iliofemoral and 10.8% in the tibiobular arteries. Next, to objectively assess the severity of IC, we measured the MWD via a progressive treadmill test on a motorized treadmill (model 2200.1 Trim-line; Hebb Industries Inc, Whitehouse, Tex). This test was carried out at a constant velocity of 3.2 km, initially on a level surface (0° incline) and then with a progressive increase of 2% in the incline every 2 minutes. The test was performed until pain prevented the patient from continuing to walk.11

Patients with other disorders that were more severe than IC, such as neuropathy, heart failure, and fracture, were not included in the protocol, and neither were those with severe ischemia at the first clinical evaluation (gangrene or ischemic pain at rest).

Sixty-two percent (312/500) of the patients were males; mean patient age was 63 years (range, 10-85 years). Only 22.8% of the patients had never smoked; the others had done so for more than half of their lifetime (mean, 23.8 cigarettes per day). The most prevalent associated conditions were systemic arterial hypertension (64.0%), diabetes mellitus (25.4%), angina pectoris (17.6%), and previous myocardial infarction (17.8%).

A program of physical activity, consisting of walking for 40 min/d 4 times a week, was prescribed. Patients were instructed to continue to walk after the onset of typical pain but before the pain reached its maximum intensity. At this point, patients should rest until the pain subsides and then start walking again to complete the time required. In face-to-face meetings, we (N.W., L.N., and R.A.R.) carefully instructed the patients about the benefits of exercise training. Also, patients were encouraged to stop smoking and were instructed about the benefits of doing so. No patient was given any type of pharmacologic therapy, but those who were using antiplatelet agents for cardiac diseases were instructed to continue this therapy.

Patients were reevaluated after 3 and 6 months, and every 6 months thereafter. Follow-up ranged from 3 months to 4 years, with an average of 18 months. At each visit, the treadmill test was performed and MWD was determined. The difference between the MWD at a given visit and that registered at the initial visit is called “the effect of treatment.”

Different levels of treatment compliance were quantified on an ordinal scale ranging from 0 to 3 at each follow-up visit by means of interviews that were always performed by one of us (N.W., L.N., and R.A.R.). Grade 3 was assigned to patients who walked regularly and did not smoke, grade 2 to patients who walked regularly but smoked, grade 1 to patients who did not smoke and did not walk regularly, and grade 0 to those who did not follow any of the instructions, that is, they continued smoking and did not walk during the entire clinical follow-up.

STATISTICAL ANALYSIS

To study the evolution of MWD over time, the average effect of treatment was calculated for the different degrees of adherence. Dispersion graphs were created to relate the length of time for which different degrees of adherence were maintained to the effect of treatment. Using statistical analysis methods, we verified whether the effect of treatment was different before and after 6 months.

We observed that 298 patients maintained the same level of treatment compliance during the study and that 202 did not. That is, at certain times during treatment, the latter patients adopted different levels of treatment. Separate statistical analyses were performed for 2 groups of patients. In the first group, only patients who maintained the same level of treatment compliance were considered (n=298). In the second group, all of the study patients were included (n=500).

Statistical analyses using 2 models of stepwise multiple linear regression were performed to verify whether there was a relation between the increase in MWD and the duration of treatment. The level of significance was 5%. Because many observations were recorded for each patient and correlation between intraindividual measurements may hinder use of the classic regression models,12 longitudinal data analysis13 was used to adjust the regression models. These statistical tools permit study of the evolution patterns of specific data over the time they are being analyzed.

RESULTS

At the initial evaluation, 97% of patients had an MWD of less than 500 m and 3% had an MWD of 500 to 800 m. Of the 500 patients, 298 maintained the same level of compliance to treatment throughout follow-up. At the first follow-up visit, 53.5% of patients had totally adhered to treatment (stopped smoking and walked); at the second visit, 57.5% of patients were in compliance.

Nineteen patients (3.8%) progressed to severe ischemia (ischemic pain at rest or gangrene), 4 of whom successfully underwent bypass surgery and 1 of whom successfully underwent primary amputation; the remaining 14 patients improved with clinical treatment. Another 15 patients underwent surgical or endovascular procedures owing to worsening or stabilization (at a disabling level) of the walking distance after at least 6 months of clinical treatment.

The first stepwise multiple linear regression model, including 298 patients who sustained the same level of treatment compliance throughout follow-up, showed that in patients with total compliance (grade 3), the effect of treatment was statistically significant during the entire period considered, and more so in the first 6 months (Table 1). In patients with grade 2 compliance, a significant improvement was detected in the first 6 months only; after that, the treatment effect was null. The effect of treatment was null for patients with compliance grades 1 and 0 throughout follow-up. The effect of treatment by compliance level for this group is also shown in the Figure.

The second stepwise multiple linear regression model, including all 500 of the patients studied, was analyzed in a similar manner as the first model (Table 2). Unlike the first model, the second model accounts for the intervals between referrals, which introduces bias into
the graphs in the Figure. The conclusions were similar, except in patients with grade 1 compliance, in whom the effect of treatment was significant over all the time taken into account (mean±SD, 7.58±1.76). However, the walking distances were shorter (7.58 m).

### Table 1. Effect of Treatment According to Treatment Compliance in 298 Patients Who Sustained the Same Level of Compliance Throughout the Study

<table>
<thead>
<tr>
<th>Treatment Compliance</th>
<th>6 mo</th>
<th>P Value</th>
<th>&gt;6 mo</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Did not smoke and walked (grade 3)</td>
<td>33.70 ±3.82</td>
<td>&lt; .001</td>
<td>4.24 ±1.41</td>
<td>.003</td>
</tr>
<tr>
<td>Smoked and walked (grade 2)</td>
<td>42.92 ±8.71</td>
<td>&lt; .001</td>
<td>1.60 ±3.50</td>
<td>.65</td>
</tr>
<tr>
<td>Did not smoke and did not walk (grade 1)</td>
<td>3.54 ±2.55</td>
<td>.17</td>
<td>3.54 ±2.55</td>
<td>.17</td>
</tr>
<tr>
<td>Smoked and did not walk (grade 0)</td>
<td>0.48 ±2.58</td>
<td>.85</td>
<td>0.48 ±2.58</td>
<td>.85</td>
</tr>
</tbody>
</table>

Patients with IC have variable expectations about improvements in walking distances. Some would like to be able to walk long distances, and others are happy if they can perform their customary daily activities. The common trait among all patients is the desire to meet this objective in the shortest time. The ideal treatment for IC would allow total regression of the walking restriction in the shortest possible time with the least risk. However, there is no therapy that safely meets all of these expected effects.

Clinical treatment is noninvasive, has practically no incidence of complications, has proven efficacy in improving walking distances, and is beneficial for the entire cardiovascular system. This approach interrupts or at least lessens the progression of arteriosclerotic disease. Therefore, clinical treatment can be considered as the initial treatment. Physical training may be performed by patients under medical guidance (unsupervised) or under the guidance of a paramedical professional (a physiotherapist or a physical educator).

In medical practice, unsupervised treatment is used most because it does not entail direct costs for the patient and it allows for practice at any time. The physician teaches the patient how to control risk factors and how to perform the physical exercises. A detailed instruction session and checking of the results are fundamental for treatment success. If carried out in this manner, unsupervised treatment is a good alternative for many patients with IC. Despite its effectiveness for most patients, in some cases success is not achieved, perhaps owing to unsuccessful treatment or inadequate physical training. Some patients stop walking too soon after the onset of pain when not exercising under supervision by a physiotherapist or a physical educator.

Supervised training seems to offer a better outcome. However, cohorts reported in the literature are small and are not representative of the total population of patients with IC. In real life, patients with IC compose a defined population with its own particular characteristics. Therefore, we decided to consider this group as a whole, and we did not reject the extremes in the sample; age, ankle-brachial index, disease severity, and initial MWD.

In our experience, patients with higher levels of restrictions resist participation in supervised training because of various psychologic, social, and economic motives. Because many patients with IC are seen at the
University of Sao Paulo and because of its effectiveness, we decided to treat them in a systematic way. As shown in this study, the level of compliance with treatment is directly related to the clinical course of the disease. The reason for a patient’s partial compliance might be the difficulty in stopping smoking. Psychologic mechanisms that affect treatment compliance must be more carefully approached to increase the level of compliance.15 Some patients performed physical training but did not stop smoking (13.1%), probably a more difficult endeavor owing to nicotine addiction.15

Our data lead us to conclude that even simple medical counseling performed over time can bring about changes in patients’ ways of life if performed in an attentive and positive manner. The period that the elective conservative initial treatment can be sustained is not based on specific scientific studies.

Imparato and colleagues,16 in 1975, studying more than 600 patients, suggested 6 months of unsupervised clinical treatment. However, this value is based on their experience and not on objective data from the literature. The only studies1,8,9 that have examined the duration of clinical treatment used supervised training and small samples. No published study, to our knowledge, has been undertaken specifically for evaluating walking capacity over time. Secondary data from these studies are used to perform some analysis of this issue. Few surveys surpass the 6-month period, and some studies have conflicting results.1,7-9

There are several differences between the present study and those mentioned previously. First, all of the other studies were undertaken in a supervised manner, whereas ours was not supervised. Second, we studied 500 patients, whereas the other studies suggesting improvement over time included no more than 20 patients each. Third, our temporal analysis covered a longer period (>12 months). Last, because we had a representative study sample, we used parametric statistical methods, which offer more reliable conclusions owing to their high sensitivity. Such differences permitted a more adequate and comprehensive statistical analysis in addition to specific conclusions for the therapeutic mode used. In addition, to avoid the variability of the absolute values of distances, statistical analysis was performed using the previously defined effect of treatment, known as the difference between the final and entry MWDs. This way, the linear regression model can be applied properly.

Regarding pharmacologic therapy, it was our intention not to use such treatment. In this way, it was possible to establish a baseline evolution for patients undergoing exercise therapy alone, free of drugs. Therefore, new studies using drug therapy could be designed, and the results could be easily compared with the present ones.

Studies in the literature on the effect of treatment for IC mostly use 2 points in time (the first and last evaluations), and their conclusions regarding treatment duration are their main drawback. Patients are usually anxious to know their prognosis and how much time is required to achieve an outcome. Physicians frequently wonder whether a poor outcome after 6 months of an exercise training program means that the treatment has failed and that another type of treatment is needed. This study addresses such questions properly, relating outcome expectations to adherence grade and treatment extent.

The stepwise multiple linear regression technique used in this study gave viability to the plotting of graphs of the effect of treatment per time unit, as shown in the Figure.

The diagnosis of IC in our patients was made at the first visit. Thus, it was not possible to state objectively when the patient’s IC had been triggered or whether this claudication was stable on admission to the hospital.

Two statistical analyses were performed in the present study. The second of these focused on data from patients who had variable treatment compliance. Using longitudinal data analysis, we calculated the evolution over time using a larger number of patients and also homogenized the patient sample regarding factors that were not individually analyzed, such as ankle-brachial index, disease severity, and MWD. The fact that both statistical analyses had similar results supports the idea that the outcome was unrelated to these factors.

There was great interpatient variability in MWD on entry. Thus, we used the effect of treatment as a more consistent variable during follow-up. Compliance also varied during treatment, and, therefore, isolated observations could not be used as predictive factors.

We detected a significant improvement in the first 6 months of clinical treatment in patients who walked, notwithstanding the association with smoking. After the first 6 months, the effect of smoking became noticeable, as patients who walked and did not smoke continued to increase their walking distance, whereas those who continued to smoke but walked did not, from there on, show any significant increase.

The mean ± SD monthly gain in the effect of treatment (MWD) after the first 6 months in the group that adhered totally to clinical treatment (grade 3) was 4.24 ± 1.41 m, which is only one eighth of the monthly gain achieved in the first 6 months; although statistically significant, this finding may not be clinically significant.

Table 2. Effect of Treatment According to Treatment Compliance in All 500 Patients Studied

<table>
<thead>
<tr>
<th>Treatment Compliance</th>
<th>≤6 mo</th>
<th>P Value</th>
<th>&gt;6 mo</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Did not smoke and walked (grade 3)</td>
<td>36.42 ± 2.61</td>
<td>&lt;.001</td>
<td>3.07 ± 1.32</td>
<td>.02</td>
</tr>
<tr>
<td>Smoked and walked (grade 2)</td>
<td>34.64 ± 5.06</td>
<td>&lt;.001</td>
<td>2.18 ± 3.22</td>
<td>.50</td>
</tr>
<tr>
<td>Did not smoke and did not walk (grade 1)</td>
<td>7.58 ± 1.76</td>
<td>&lt;.001</td>
<td>7.58 ± 1.76</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Smoked and did not walk (grade 0)</td>
<td>0.28 ± 2.18</td>
<td>.90</td>
<td>0.28 ± 2.18</td>
<td>.90</td>
</tr>
</tbody>
</table>

Footnotes:

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Regarding patients who did not practice physical training (grades 1 and 0), the analysis of patients who followed an equal level of compliance to treatment during the entire study disclosed that there was no statistically significant improvement in MWD. However, when using the second statistical test of stepwise multiple linear regression, which includes all patients, we observed that individuals who did not walk and did not smoke had a mean ± SD progressive improvement of 7.58 ± 1.76 m/mo during the entire study. Again, we believe that this statistically significant improvement has poor clinical significance, but it is better than that of patients who did not walk and continued to smoke (and did not show any improvement in either of the statistical methods used).

Based on the submitted data, we constructed a table of the expected values of MWD for given time lapses, initial walking distances, and levels of treatment compliance (Table 3). This table allows the physician to give patients who are beginning clinical treatment an idea of the walking distances they might achieve over time in accordance with the level of compliance to the adopted treatment. Accordingly, these data provide motivation for patients and their physicians to implement lifestyle changes to improve walking distances. The table also provides a realistic expectation of outcomes if changes are not instituted. In addition, this study could provide solid support for moving on to other therapies if an exercise program is not successful after the expected period. Finally, we believe that supervised exercise programs could provide even better outcomes than these unsupervised programs. New studies designed to compare these 2 methods are yet to be performed, to our knowledge.

In conclusion, patients who adhere totally to clinical treatment (walk and do not smoke) exhibit an increase in MWD throughout treatment. The mean monthly increase achieved in the first 6 months is substantially greater than that after 6 months. Patients who adhere to physical training but continue to smoke exhibit a significant increase in MWD in the first 6 months; however, after 6 months, the effect of treatment in these cases is null.

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Table 3. Expected Maximum Walking Distances for the Given Time Lapses, Initial Distances, and Levels of Treatment Compliance

<table>
<thead>
<tr>
<th>Treatment Compliance</th>
<th>Initial Walking Distance, m</th>
<th>3 mo</th>
<th>6 mo</th>
<th>9 mo</th>
<th>12 mo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Did not smoke and walked (grade 3)</td>
<td>100.0</td>
<td>201.1</td>
<td>302.2</td>
<td>340.4</td>
<td>353.1</td>
</tr>
<tr>
<td>Smoked and walked (grade 2)</td>
<td>100.0</td>
<td>228.8</td>
<td>357.5</td>
<td>357.5</td>
<td>357.5</td>
</tr>
<tr>
<td>Did not smoke and did not walk (grade 1)</td>
<td>100.0</td>
<td>100.0</td>
<td>100.0</td>
<td>100.0</td>
<td>100.0</td>
</tr>
<tr>
<td>Smoked and did not walk (grade 0)</td>
<td>100.0</td>
<td>300.0</td>
<td>300.0</td>
<td>300.0</td>
<td>300.0</td>
</tr>
</tbody>
</table>

REFERENCES