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Original

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Instrumented gait analysis for an objective pre/post assessment of tap test in normal pressure hydrocephalus

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ABSTRACT.

Objective: To present an objective method to evaluate gait improvements after tap test in idiopathic normal pressure hydrocephalus (iNPH). Tap test is often used to prognosticate shunt responsiveness, although test accuracy is limited by the lack of quantitative outcome measures.

Design: Retrospective analysis of gait data.

Setting: Public tertiary care center, day hospital. Gait analysis was performed before and 2-4 hours after tap test.

Participants: 60 iNPH patients and 50 age and sex matched controls (used to obtain reference intervals). From an initial referred sample of 79 patients, we excluded those unable to walk without walking aids ($n = 9$) or with incomplete (pre/post tap test) gait data ($n=10$). Thirteen out of 60 patients were shunted and then reappraised after 6 months.

Intervention: Not applicable.

Main Outcome Measures: Mahalanobis distance from controls, before and after tap test. Eleven gait parameters were combined in a single quantitative score. Walking velocity was also evaluated, since it is frequently used in tap test assessment.

Results: Patients were classified as: (A) tap test responders ($n=22$ patients, 9 of them were shunted), or (B) not suitable for shunt ($n=38$ patients, 4 of them were shunted). In group A, 9 out of 9 patients improved after shunt. In group B, 3 out of 4 patients did not improve. Gait velocity increased after tap test in 53% of responders and in 37% of patients not suitable for shunt.

Conclusions: The new method is applicable to the clinical practice and allows for selecting tap test responders in an objective way, quantifying the improvements. Our results suggest that gait velocity alone is not sufficient to reliably assess tap test effects.

Key Words: Gait analysis; tap test; normal pressure hydrocephalus; Mahalanobis distance; gait velocity

List of abbreviations:

CSF: cerebrospinal fluid

ELD: external lumbar test

iNPH: idiopathic normal pressure hydrocephalus

MD: mahalanobis distance

MRI: magnetic resonance imaging

ROM: range of motion (dynamic)

TT: tap test

INTRODUCTION

Normal pressure hydrocephalus is a neurologic condition characterized by an enlargement of the ventricles and by a clinical picture named as Hakim triad (gait impairment, mental deterioration, and urinary incontinence).[1-9] The symptoms of the disease can be improved by the shunting of cerebrospinal fluid (CSF). Shunt surgery is routinely applied to selected patients after a careful clinical assessment of the potential risks and benefits.[10]

The diagnosis relies on convergence of clinical history, physical examination and brain imaging showing a ventricular enlargement.[2, 4, 8] Despite the classic clinical picture, the daily diagnosis of the disease is complicated because of the variability in its clinical presentation and course. In fact, other frequent conditions of the elderly may present similarly to iNPH such as cerebrovascular disease, neurodegenerative disorders, spinal stenosis, primary urological disorders.[4] Supplemental prognostic test such as intra-cranial pressure monitoring, external lumbar drainage test (ELD), measurement of CSF outflow resistance, CSF tap test (TT) have been employed in clinical practice in order to attain a higher specificity and sensitivity for diagnosis of iNPH and to achieve a reliable prediction of a positive shunt response.[11-12]

Although the CSF tap is regarded as less sensitive than ELD,[8] it is largely employed because considered as an easy, safe, inexpensive and not time consuming test. A positive response of gait disturbances to a 40-50 ml TT is generally considered to have a high degree of certainty for a favorable response to shunt placement. The guidelines of the Japan Neurosurgical Society,[6]

and NPH Study Group,[5, 10, 12] point out the positive predictive value of TT (73-100%).

Nevertheless, they suggest that a negative result of CSF tap should not exclude patients from surgery because of the test's low sensitivity.

In spite of the widespread use of TT to determine shunt responsiveness, instrumented gait analysis is very seldom used as an outcome measure.[13-16]

iNPH patients frequently show a reduced gait velocity and a diminished and highly variable step length. Specific features of their gait disturbance are a broad based gait pattern with outward rotated feet and a diminished height of steps.[15] They also show an augmented duration of the period of double support, i.e., the percentage of the gait cycle in which both feet are in contact with the ground.[16] This feature is often referred to as “magnetic gait”, to highlight the patient's difficulty in raising the foot from the floor during limb advancement.

Gait improvements after TT are often evaluated by clinicians in a subjective way or performing simple walks such as the 10-m test.[17-21] The latest is equivalent to measure the patient's gait velocity.

Instrumented gait analysis may be an important tool to objectively assess gait changes after TT, thus helping clinical decision in shunt candidate selection.[16] Recent advances in gait analysis highlighted the importance to evaluate uninterrupted walking trials, lasting 2-3 minutes.[22-26]

This allows for a reliable evaluation of gait parameters since 50-150 gait cycles are collected and analyzed for each patient.

The aim of this work is to present an objective method for selecting TT responders, based on gait parameters automatically extracted from an instrumented walk.

MATERIALS AND METHODS

Participants

Seventy-nine consecutive patients diagnosed with clinical suspected iNPH were referred to our gait analysis laboratory from the neurosurgery or neurology units, between 2011 and 2014, to evaluate gait improvements after TT. The patients generally showed a short-stepped “magnetic” gait, cognitive disturbances and, in many cases, urinary incontinence. All patients were submitted to a neuropsychological evaluation and to a brain MRI (magnetic resonance imaging). Patients reached our unit early in the morning and were assessed a first time by instrumented gait analysis. Then they underwent a spinal CSF tap of 30-50 ml in the neurosurgery unit. From 2 to 4 hours after TT, patients’ gait was assessed a second time with the same procedure.

We studied retrospectively our gait analysis database. Patients were excluded from the study when they were unable to walk without walking aids ($n = 9$), when they did not complete the entire protocol ($n = 9$ missed the post-TT evaluation) or when data were corrupted ($n = 1$). Sixty patients (44 males, 16 females) of mean age 73 ± 8 years were considered for the analysis.

Thirteen of these 60 patients underwent shunt surgery. All except one were assessed a third time by gait analysis, 6 months after surgery. The remaining subject could not perform the gait test since he was not able to walk any more.

The selection of patients to be shunted was based on a clinical report summarizing the more relevant gait changes observed after TT. The report included the subjective impressions of the team on the movement fluency during gait. It also included the perceived sensations of patients (or their relatives): they were interviewed by phone about gait, memory, and continence within the 24 hours after TT.

A control group of 50 volunteers (30 males, 20 females) of similar age (mean: 71 ± 12 years) was recruited from the local community to obtain reference intervals, in normal health conditions, for the studied gait parameters. Controls were clinically assessed prior to the gait analysis test to exclude the presence of orthopedic or neurological disorders that could affect their gait. They performed the instrumented gait test only once.

The research reported in the paper was undertaken in compliance with the ethical principles of the Helsinki Declaration.

Experimental set-up

The instrumented test was performed by an easy-to-use, cheap and reliable multichannel recording system^a used in clinical gait analysis.[22-26] Three foot-switches were fixed under the heel, the first and fifth metatarsal heads of each foot sole (Fig. 1a), and a knee goniometer was attached to the lateral side of each leg (Fig. 1b). Subjects were instructed to walk barefoot at self-selected speed. They walked back and forth over a 9-m pathway for 2.5 minutes (Fig. 1c). The system recorded, for each lower limb, the foot-floor contact signal and knee flexion-extension angle (in the sagittal plane). The sampling frequency was 2 kHz. The foot-floor contact signal was debounced and converted to a 4-level signal by the system software, coding the gait phases: heel contact, flat-foot contact, push off and swing. Then, the signal was segmented into separate gait cycles as described in Ref. [24]. The knee kinematic signal was low-pass filtered (FIR filter, 100 taps, cut-off frequency of 15 Hz). In the analysis we considered only the walking along a linear path, discarding the strides related to direction changes. This is automatically managed by the system software. More specifically, a multivariate statistical filter (Hotelling t-test, $\alpha = 0.05$) discarded the “outlier” cycles, i.e., strides with abnormal timing, like those relative to

deceleration, reversing, and acceleration. A video recording of the subject's walk was also captured, synchronous with gait signals. Subject preparation and signal acquisition overall required about 15 minutes.

Gait parameters

For each foot, the system identifies the time events of the four gait phases (Fig. 2). It also calculates the double-limb support, defined as the percentage of the gait cycle in which both feet are in contact with the ground.[27] Furthermore, it calculates the dynamic Range of Motion (ROM) of the knee joint, defined as the difference between the maximum and minimum flexion-extension angle observed during the gait cycle.

Summarizing, for each subject, we considered 11 parameters:

- heel contact duration (left and right), as percentage of gait cycle
- flat-foot contact duration (left and right), as percentage of gait cycle
- push off duration (left and right), as percentage of gait cycle
- swing duration (left and right), as percentage of gait cycle
- double-limb support duration, as percentage of gait cycle.
- dynamic ROM (left and right), degrees

The gait parameters differences between patients and controls were estimated by Student's *t*-tests (two-sample, 2 tails, level of significance $\alpha=0.05$).

Mahalanobis distance from controls and rule to select TT responders

A preliminary analysis showed that no single parameter was sufficient to describe a patient's gait, but all of them were relevant. However, since our aim was to compare the patient's

performance before and after TT, we found important to obtain a single indicator “scoring” the patient’s gait, rather than analyze many parameters separately. To this purpose, we calculated the Mahalanobis Distance (MD) of each patient from the group of controls,[28] using the 11 gait parameters defined above. This multivariate distance describes how much a patient’s performance deviates from controls. We scored the performance of each patient: a) before TT, b) after TT, and, when the patient was operated, c) after shunt.

Then, we established if a patient’s gait, before TT, was altered with respect to controls. We defined “not suitable for TT” those patients walking like normal subjects. In fact, it is reasonable to avoid TT (and surgery) in patients lying within the “range of normality”. The upper limit of this range was defined as the controls’ MD mean + 3 standard deviations (SD). Among patients suitable for TT, we defined “TT responders” those who decreased their MD of at least 10%, after TT, and “non-responders” those who did not. Notice that to decrease MD (from controls) means getting closer to normal gait.

We used custom software routines^b to calculate MDs and select TT responders. These routines are available upon request.

Gait velocity

We calculated the gait velocity before and after TT using the video-recordings. We clocked each patient’s passage through the 9-m walkway (see Fig. 1c). More specifically, we measured the time that the patient needed to walk from A to B, then from B to A, then from A to B again, etc..., timing each passage with the exclusion of direction changes. The average velocity was defined as the total distance walked in a straight line divided by the total time required to go

through it. Similarly to what it is suggested in literature,[21] we defined “velocity improvement” an increase in the velocity, after TT, of at least 10%.

Group matching

We applied a Student *t*-test (two-sample, 2 tails, level of significance $\alpha=0.05$) to check the matching between iNPH and control group for age. A chi-square test for homogeneity of proportions was used to study the differences in the male/female number between groups ($\alpha=0.05$). The iNPH and control groups didn't show a significant difference for age ($p = 0.35$) or sex ($p = 0.14$).

Sensitivity analysis

In the presented methodology based on the MD we introduced two thresholds: 1) the limit defining the range of normality (mean + 3 SD), 2) the minimum MD percentage change (10%) discriminating a significant improvement after TT. The choice of the values assigned to these thresholds is reasonable, but subjective.

In order to test the robustness of the choice made, we performed a sensitivity analysis,[29] studying to what extent the results obtained depend on the chosen thresholds.

RESULTS

The average distance that patients walked within 2.5 minutes was 80 ± 40 m, considering only the straight path. The gait parameters of the subjects included in the study are reported in Table 1. Patients showed a decreased velocity, swing, and knee ROMs, and an increased double support, and flat-foot contact with respect to controls, both pre and post TT.

Selection of TT responders using MD

We selected 41 patients suitable for TT and 19 not suitable for TT. Among the 41 suitable for TT, 22 responded to TT and 19 did not. Hence, overall 38 patients were not suitable for shunt (19 not suitable for TT and 19 non-responders).

In Fig. 3 we reported, for each patient, the MD value before TT (indicated by a star) and after TT (indicated by a triangle). We also reported the MD value after shunt (indicated by a circle), when applicable. The range of normality spans between 0 – 26 (arbitrary units, a.u.). The horizontal line indicates the normality upper limit. The higher the MD value, the worse is the patient's gait impairment. Patients "suitable for TT" are those indicated by stars above the horizontal line.

Among them, TT responders are highlighted by a rectangle. The more the triangle is far from the star (below it), the higher the gait improvements are, due to the CSF tap.

Thirteen patients underwent shunt surgery. Nine of them fell in the TT-responder group (patients # 7, 12, 14, 18, 19, 28, 39, 44, 54). Four of them fell in the group "not suitable for shunt" (indicated by an arrow in Fig. 3). More specifically, of these four patients, 1 belonged to the group "not suitable for TT" (patient # 58) and 3 to the group of non-responders (patients # 3, 41, 57).

In the group of TT responders, all the patients improved after shunt (9/9). Their MD decreased, on the average, from 147 ± 144 a.u. (before TT), to 84 ± 95 a.u. (after TT) and further decreased to 42 ± 40 a.u. after shunt. Hence, their improvements after shunt were, on the average, higher than those after TT. More specifically, the MD percentage decrement was $44 \pm 21\%$ after TT and $59 \pm 27\%$ after shunt, respectively. In the group of "not suitable for shunt" 2/4 worsened their

condition (one was unable to walk 6 months after shunt), 1/4 did not change his condition, and 1/4 improved after shunt (see discussion). Figure 4 outlines these results.

Gait velocity

Gait velocity improved in 53% of TT responders and in 37% of patients not suitable for shunt. More specifically, focusing on this latest group, velocity improved in 29% of patients classified as “not suitable for TT” and in 44% of “non-responders”.

For what concerns the subgroup of 13 patients that were shunted, the situation is the following. On the average, the velocity increased after TT from 0.5 ± 0.3 m/s to 0.7 ± 0.2 m/s, and further increased after shunt (0.8 ± 0.2 m/s). Among the 9 patients classified as TT responders, 3 did not improve their velocity after TT. Among the 4 patients classified as “not suitable for shunt”, 2 improved their velocity after TT, but they didn’t improve, after shunt, neither their velocity nor their MD.

Sensitivity analysis

We varied the first threshold (defining the limit of normality) in the range [mean + 2.5 SD, mean + 3.5 SD]. When this first threshold was set equal to (mean + 2.5 SD) 3 more patients were classified as TT-responders (error = $3/60 = 5\%$), while considering (mean + 3.5 SD) no change was obtained in the classification of TT responders (error = 0%). Varying the second threshold (minimum MD percentage decrease) in the range 5-15% no change was obtained in the classification of TT responders (error = 0%). None of the above mentioned thresholds’ variations altered the results presented on the 13 patients after shunt (error = 0%).

DISCUSSION

Clinicians have not reached a consensus on the usefulness and predictive value of TT. The sensitivity and specificity reported are very variable from study to study.[2, 5, 6, 8, 11, 12] A major issue in establishing the prognostic value of CSF tap is the method applied to document gait changes. The use of inadequate and/or subjective outcome measures may be a critical aspect.[13-14] Furthermore, if gait improvements after CSF tap are small, they can be missed by a clinical examination not supported by an instrumented test.[13]

We presented an objective method to score the patient's gait performance, before and after TT, based on the measure of parameters extracted from an instrumented gait analysis lasting 2-3 minutes. We demonstrated that this approach is feasible in the clinical practice. We are now routinely applying gait analysis for TT assessment in our center.

We hypothesized that a functional improvement may be expected only in patients with clinically appreciable gait disturbances. Hence, it is useless to perform TT in those whose gait is already in the range of normality. Therefore, a quantitative gait assessment before TT allows avoiding unnecessary CSF taps.

Patients that responded to TT were 37%. All the responders that were shunted (9 of 9) improved after surgery. Among patients non-candidate for shunt only 1 of 4 improved after shunt.

However, a deeper examination of this patient's clinical record revealed that he underwent an unusual CSF tap of less than 20 ml. Such a limited tap was probably not sufficient to produce a noticeable clinical change.

Literature reports that improvements after TT seem to be positively correlated with improvements after shunt.[12] Our results confirm this finding although more data would be needed to explore this correlation. However, the possibility to quantify improvements after TT,

objectively and accurately, may be important to prognosticate the level of improvement after surgery.

Patient's walking velocity is one of the most common measurement parameter used for evaluating TT responsiveness, and it is frequently assessed by the 10-m test. However, caution should be taken when considering the velocity as the only parameter for describing TT responsiveness. Our results showed that velocity improved approximately in one half of responders and in one third of patients non-candidate for shunt. This suggests that it is probably not sufficient to measure the velocity for selecting shunt candidates. An explanation of this finding may be that velocity is biased by confounding factors, both in a positive or negative way. Among these factors there are: 1) habituation effect, i.e. the fact that patients undergo the walking test for a second time during the day, perhaps feeling more confident and secure, 2) fatigue effect, since they are asked to fast several hours; 3) pain, since post-lumbar puncture pain may negatively affect the gait function.[21]

Measuring a gait parameter by an automatic analysis of many strides improves the parameter's estimation accuracy.[22] Furthermore, choosing multiple parameters directly correlated to gait dysfunctions provides a more reliable assessment than considering a single parameter. The parameters selected for this study well represent the iNPH gait dysfunctions. An increase in the double-limb support duration is directly correlated to "glue-footed" or "magnetic gait", while a reduced knee flexo-extension is correlated with the attitude of walking with broad-base strides of reduced length. On the other hand, we decided to discard cadence from the analysis. Cadence is defined as the number of strides per minute. We found that this parameter may be misleading for the iNPH population, since pre/post changes may be difficult to interpret in many practical

situations. As an example, cadence may increase if: 1) velocity increases (meaning a functional improvement) or 2) step length reduces (functional worsening).

Study Limitations

We did not apply this technique to patients needing mobility aids (canes or walkers). This is only a partial limitation since some of the patients using walking aids before TT were able to walk without them after TT. In these cases, the clinical improvement was evident without the need for an instrumented gait analysis.

Among the 22 responders only 9 were shunted. The remaining 13 patients were not operated due to serious comorbidities (lung cancer, hepatocellular carcinoma, severe cardiomyopathy), or because they asked to procrastinate the intervention at a later date.

CONCLUSIONS

We propose a new method to evaluate the effects of the CSF lumbar tap on gait. The method is promising both in terms of objectiveness and reliability. This approach is based on the use of many gait parameters specifically studied to describe iNPH walking features, summarized in a single indicator, i.e. the Mahalanobis distance of a single patient from controls. Furthermore, our findings suggested that gait velocity alone may not be sufficient to establish responsiveness to tap-test. Hence, simple tests like the 10-m test may not be sufficiently reliable as an outcome evaluation of CSF tap and may be the cause of the actual limited predictive value of TT.

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Suppliers

a. STEP32; Demitalia, sold by Medical Technologies, Via Bogetto 8, Torino, IT 10144.

<http://www.medicaltec.it/STEP32.html>

b. MATLAB®; The MathWorks Inc, 3 Apple Hill Dr, Natick, MA 01760-2098.

Table 1 - Gait parameters for iNPH patients and controls.

Gait parameters	iNPH patients (<i>n</i> = 60)		Controls (<i>n</i> = 50)
	PRE TT	POST TT	
Velocity (m/s)	0.6 ± 0.2 **	0.7 ± 0.2 **	1.0 ± 0.1
1 Double support (% gait cycle)	30.9 ± 9.7 **	27.8 ± 7.8 **	17.6 ± 4.4
2 Heel contact, left (% gait cycle)	7.1 ± 4.6	7.0 ± 4.8	6.0 ± 2.8
3 Heel contact, right (% gait cycle)	7.3 ± 7.0	8.3 ± 6.9*	5.6 ± 2.3
4 Flat foot contact, left (% gait cycle)	40.9 ± 10.0 **	39.6 ± 8.8 **	33.5 ± 5.7
5 Flat foot contact, right (% gait cycle)	40.5 ± 11.0 **	37.4 ± 9.0 *	33.6 ± 6.0
6 Push-off, left (% gait cycle)	17.8 ± 6.8	17.8 ± 6.3	19.5 ± 3.8
7 Push-off, right (% gait cycle)	17.6 ± 6.3	17.9 ± 6.9	19.4 ± 4.7
8 Swing, left (% gait cycle)	34.1 ± 5.1 **	35.6 ± 4.6 **	41.0 ± 2.4
9 Swing, right (% gait cycle)	34.6 ± 5.4 **	36.3 ± 4.3 **	41.3 ± 2.7
10 Knee ROM, left (°)	34.3 ± 7.8 **	34.7 ± 7.4 **	45.9 ± 8.1
11 Knee ROM, right (°)	36.5 ± 8.7 **	37.4 ± 7.6 **	44.3 ± 8.8

Values are mean ± standard deviation. Significant differences between iNPH patients and controls are indicated with *(*p* < 0.05) or **(*p* < 0.001).

Fig. 1. (a) Foot-switches placed under foot sole. (b) Knee goniometer measuring the joint angle in the sagittal plane. (c) Walking path.

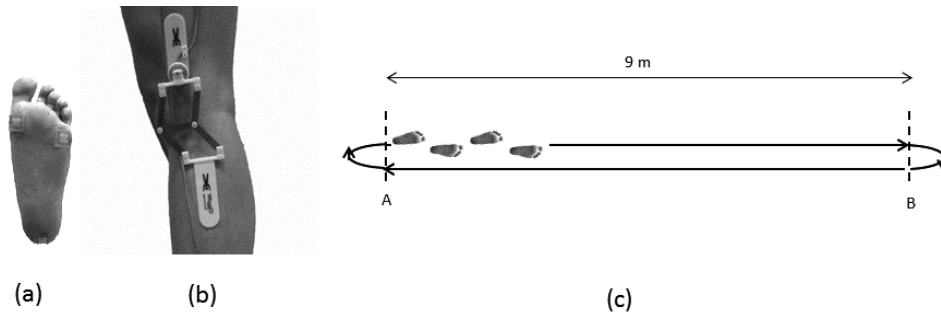


Fig. 2. Schematization of gait phases (right foot). A dark circle under the foot sole indicates a closed foot-switch.

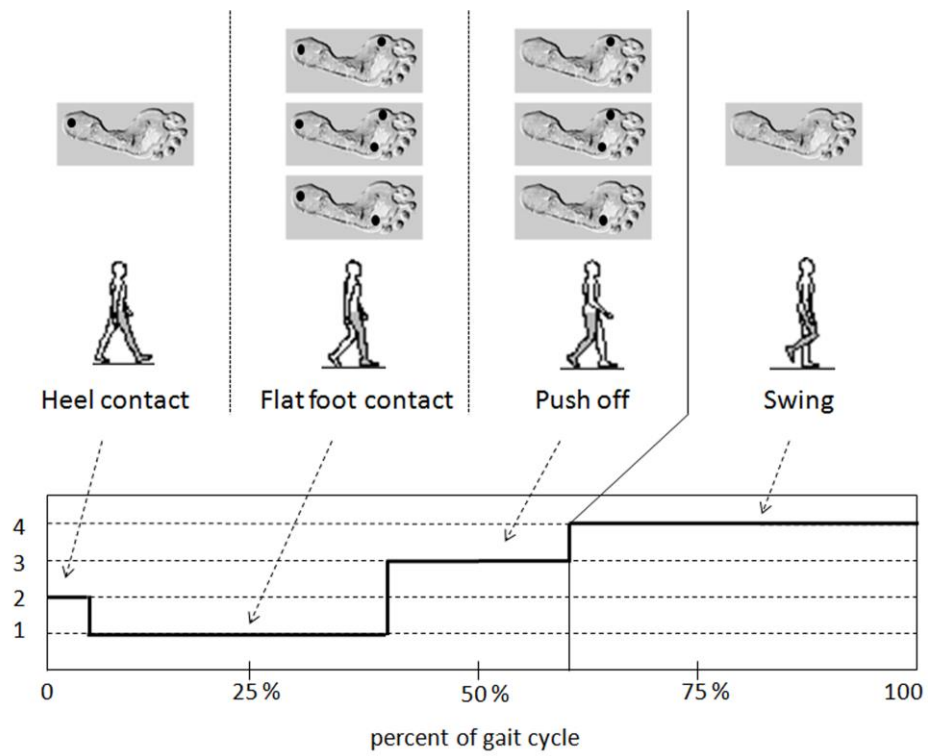


Fig. 3 Pre and post tap-test Mahalanobis distance (MD), for each patient. Post-shunt MD is also displayed, when applicable. Rectangles indicate tap test responders. An arrow indicates the operated patients classified as not suitable for shunt. The horizontal line delimits the range of normality.

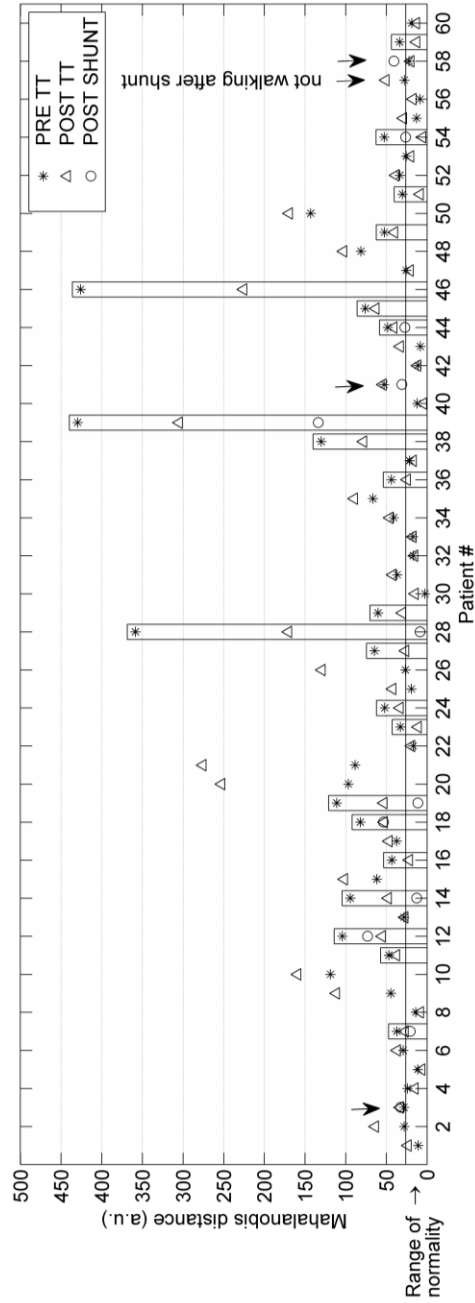


Fig. 4 Schematization of the study results.

