Rehabilitation Practice and Science

Volume 15
Issue 1 *Taiwan Journal of Physical Medicine and Rehabilitation (TJPMR)*

Article 9

12-1-1987

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Recommended Citation

Yang, Baii-Jia; Chen, Han-Shiang; Lai, Jin-Shin; Wong, Pui-Lan; and Tsai, Tun-Jun (1987) "Cardiopulmonary Function in the Long Term Hemodialysis Patients during Bicycle Exercise," *Rehabilitation Practice and Science*: Vol. 15: Iss. 1, Article 9.
DOI: https://doi.org/10.6315/3005-3846.1724
Available at: https://rps.researchcommons.org/journal/vol15/iss1/9

長期血液透析尿毒症患者之運動心肺功能研究

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長期血液透析之尿毒症患者，雖然病情穩定，仍有貧血、動脈硬化及心肺功能降低等問題。本文就19位男性，及11位女性尿毒症患者在血液透析後18至36小時，給予漸增性脚踏車運動測驗，直接測量其最大運動心肺功能，並與43位男性及9位女性正常年輕人作比較。其結果顯示尿毒症患者不論男女，其最大攝氧量或單位體重最大攝氧量皆明顯小於正常人。男性患者之單位體重最大攝氧量平均值爲 21.4ml／kg／min，僅及正常男性平均值之 42.6％，而女性患者之平均值爲 16.6ml／kg／min 爲正常女性平均值之 55.5％，此種現象和最高心跳率及最大氧脈皆降低有關，而最大呼吸交換系數（R）與正常人相似，顯示這些患者已盡力運動到非常氣喘的程度。最高心跳率的降低可能與年齡及自主神經病變有關。至於最大氧脈及最高血液乳酸濃度仍顯著低於正常人，可能和貧血，肌肉量，肌肉內細胞酵素，心臟收縮功能不佳等因素有關。因此如何改進尿毒症症患者之心肺功能值得更深入研究。

Key words：hemodialysis, bicycle exercise, maximum O_2 consumption.

前　言

目前長期血液透析仍是對尿毒症患者最有效可行的一種治療方法，其存活率已大爲提高至超過10年[1]，但是仍有嚴重貧血，體力衰退，高血壓，不正常血脂，碳水化合物代謝的問題存在[4]，根據Harter[2] 等人的研究顯示足量的運動可以提高最大攝氧量達 20 － 25 ％，同時可以改善碳水化合物及脂肪的代謝[4]，降低高血壓[3]，升高血紅素及血比容，同時對於心理健康也有相當的助益。因此我們希望對國內尿毒症患者，在長期血液透析病情穩定的情況下，給予漸增性運動功能測驗，以便了解其體能狀況，同時也爲進一步之運動治療計劃之根據。

材料與方法

本研究之對象爲19位男性及11位女性尿毒症患者，其接受血液透析的時間平均爲28個月（5～144個月）。在接受血液透析後18～36小時，病情穩定的情況下，施予漸增性脚踏車運動測驗（圖１）其增加運動量的方式爲前三分鐘保持固定之10瓦特（watt），以後每分鐘固定增加10瓦特直到無法保持定速踩動爲止。運動測驗時以面罩收集其吐出氣體，並以MGC－2000 系統測量其攝氧量（VO_2），換氣量（VE）及心跳率（HR），同時以示波器連續監視其心電圖之變化，以免發生危險。運動後五分鐘抽靜脈血檢驗其血液乳酸濃度。另有正常男性43位及女性19位（其基本資料如表１），作爲對照組。這些長期尿毒症患者之腎臟病因之分析如表２。

結　果

大部份尿毒症患者在劇烈的脚踏車運動中

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，首先感到下肢肌肉酸痛無力，氣喘，無法再繼續運動下去，而非心跳加快無法承受或胸痛，且其運動心電圖都沒有心肌缺血的變化。僅有部份本來有高血鉀症者，可見其特異性心電圖變化。運動後大部份患者情況良好，僅一位患者有噁心頭昏的現象。運動後之患者都沒有明顯出汗的現象，此爲其與正常人不同者。由表 1 顯示尿毒症患者的體型與正常人相似。但由表 3 可見其單位體重最大攝氧量男性之平均値爲 21.4 （ ± 5.5 ）ml／kg／min ，女性之平均值爲 16.6 （ ± 2.8 ）ml／min／kg ，分別爲正常男性平均値的 42.6 ％ 及正常女性平均値的 55.5 ％。最大換氣量，最高心跳率，最大氧脈，最大潮氣量，及最高血液乳酸濃度之平均値亦明顯低於對照組。而最大呼吸系數則與正常人相似，顯示這些尿毒症患者確實已盡力運動到非常氣喘的程度。由圖 2 及圖 3 ，可見血紅素及血比容在尿毒症患者皆顯著降低，且與單位體重最大攝氧量成顯著線性相關（ $r=0.521$ ，$P<0.05$ ）（ $r=0.491$ ， $P<0.05$ ）血紅素及血比容愈高則單位體重最大攝氧量愈大。而血液肌氨酸酐濃度在尿毒症患者亦相當升高，但與單位體重最大攝氧量則無顯著線性相關（圖 4 ）$r=0.245327$ ，$P>0.1$ ）。

討　論

本研究由脚踏車運動所測得的單位體重最大攝氧量，男性尿毒症患者之平均值爲 21.4 （ ± 5.5 ）ml／kg／min及女性尿毒患者之平均値爲 16.6 （ ± 2.8 ）ml／kg／min 與 Harter [2] 等人之報告利用電動跑道測出尿毒患者男女混合（男性 8 人，女性 5 人）之平均值22 （ ± 2 ）ml／kg／min比較，可見脚踏車運動之單位體重攝氧量較偏低，與國外報告[7]之正常人模式，二者相差約 5 —15 ％相符。最大攝氧量以電動跑道運動方式測得者爲最高，其次爲阻力漸增式脚踏車[6]，最低的是手搖車，主要是因爲其動用的肌肉群不同，由於尿毒症患者手上皆有動靜脈導管（ A —V shunt ），所以我們採用以動用下肢肌肉爲主的脚踏車漸增阻力運動方式來測驗尿毒患者的體能，較爲安全。

由表一可見尿毒症患者之體型與常人相似，但是最大攝氧量均明顯下降，男性患者平均僅爲正常人之 42.6 ％，而女性患者平均也僅達正常人之 55.5％而已。與國外報告相近[8]。主要是由於最高心跳率、最大氧脈及心臟收縮排出量等幾個因素的衰退引起的。以男性尿毒症患者來看，最高心跳率爲 148.3 ± 24.4 bpm，爲正常人的 75.9 ％，而最大氧脈 8.5 ±1.8 ml／beat ，則爲正常人的 56.7 ％。而最大呼吸交換系數顯示尿毒患者與正常人極爲接近，這表示尿毒症患者確定已盡力運動到非常氣喘的程度。所以最高心跳率和最大氧脈的降低確與患者之疾病有關，而非運動時沒有盡力而爲。

以最高心跳率來看，雖然與年齡[9]有關，但是這樣明顯的心跳率下降，則非單純年齡因素所造成，可能是尿毒症患者交感神經異常[8]引起的，在尿毒症患者身上，我們可以發現經過劇烈運動後，却沒有明顯出汗的現象，這也是自律神經失調的現象，可與最高心跳率降低互相印証。

最大氧脈的明顯降低在男性尿毒症患者爲正常人的 56.7 ％——這是使尿毒症患者最大攝氧量降低的主因。而其決定因素則爲血紅素量的多寡，組織攝氧能力的強弱，肌肉組織量的多少與心動排出量的大小。而由圖二、三可知尿毒症的病人有相當嚴重的貧血，血紅素、血比容皆下降。所以對最大氧脈的降低影響極大。其次肌肉細胞內無氧酵素和氧化酵素失調[10][11]導至肌肉收縮力差，及肌肉量的減少，不只影響最大氧脈使其攝氧量降低，也導至最高血液乳酸濃度的下降。根據 Harter [2]的報告，經過一年適量的運動訓練，單位體重最大攝氧量可增加 20 ～ 25 ％，因此我們可預測尿毒症患者平常的運動量有由於疾病的關係而大量降低的可能[5]，也就是所謂廢用性萎縮的現象。而這些因素也就是導至尿毒症患者心肺功能降低的原因。因此，如何改善尿毒症患者的運動心肺功能値得作更深入的研究。

表 1 尿毒症患者及正常人接受漸增式運動測驗者之基本資料。

	男性		女性	
	尿毒症患者	正常人	尿毒症患者	正常人
人數	19	43	11	9
年齡(歲)	39.0±10.3	22.6±5.1	36.7±8.9	26.0±8.5
身高(公分)	167.1±5.3	169.5±5.3	156.4±3.8	155.6±3.8
體重(公斤)	58.6±7.4	61.0±6.5	46.5±8.0	46.3±4.7

表 2 尿毒症患者(30例)之腎病診斷

Renal diagnosis	Case No.
1. Chronic glomerulonephritis	20
2. Polycystic kidney	1
3. Nephrotic syndrome	1
4. Malignant hypertension	1
5. Gouty nephritis	1
6. Chronic pyelonephritis	1
7. Eclampsia	1
8. IGA nephropathy	1
9. Unknown	3

表 3 對尿毒症患者及正常人以漸增性運動量施行脚踏車運動測驗之結果

	男性		女性	
	尿毒症患者	正常人	尿毒症患者	正常人
最大攝氧量(ml/min)	1248±306	2933±520	769±166	1385±262
單位體重最大攝氧量(ml/kg/min)	21.4±5.5	48.3±7.9	16.6±2.8	29.9±4.3
最大換氣量(ℓ/min)	60.3±20.6	111.0±26.9	35.6±6.4	60.0±11.0
最高心跳率(bpm)	148.3±24.4	195.3±11.6	142.4±17.2	183.4±9.7
最大氧脈(ml/beat)	8.5±1.8	15.0±2.7	5.4±1.0	7.5±1.2
最高血液乳酸濃度(mg/dl)	46.8±22.5	90.1±25.4	31.6±9.3	65.9±17.8
最大呼吸交換係數(R)	1.25±0.14	1.11±0.10	1.22±0.12	1.24±0.08
最大潮氣量(ml/breath)	1681±369	2269±364	1025±191	1252±243
最高呼吸率(breath/min)	36.0±8.8	49.4±10.8	35.9±8.0	48.6±4.3

圖 1

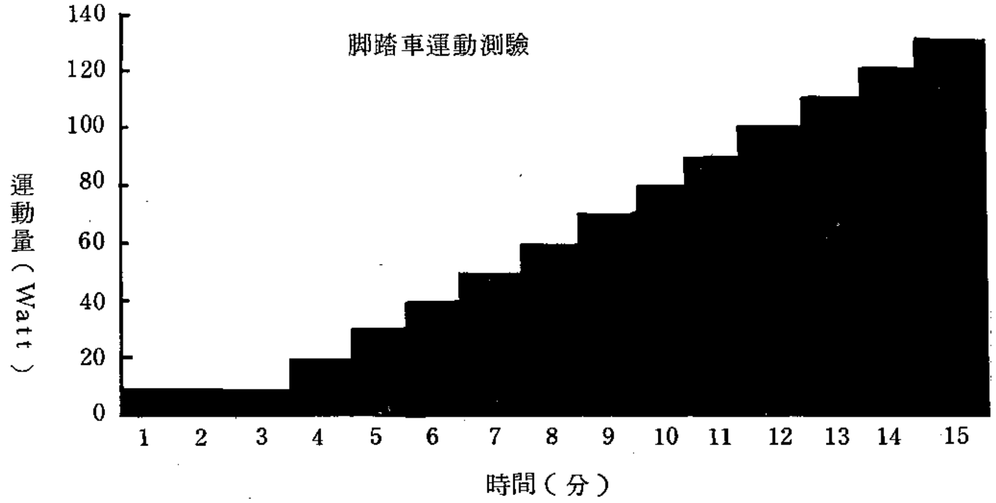

圖 1　脚踏車運動測驗之運動量給予方式爲前三分鐘均爲10.瓦特，以後每分鐘增加10.瓦特，直到受測者無法承受之運動量爲止。

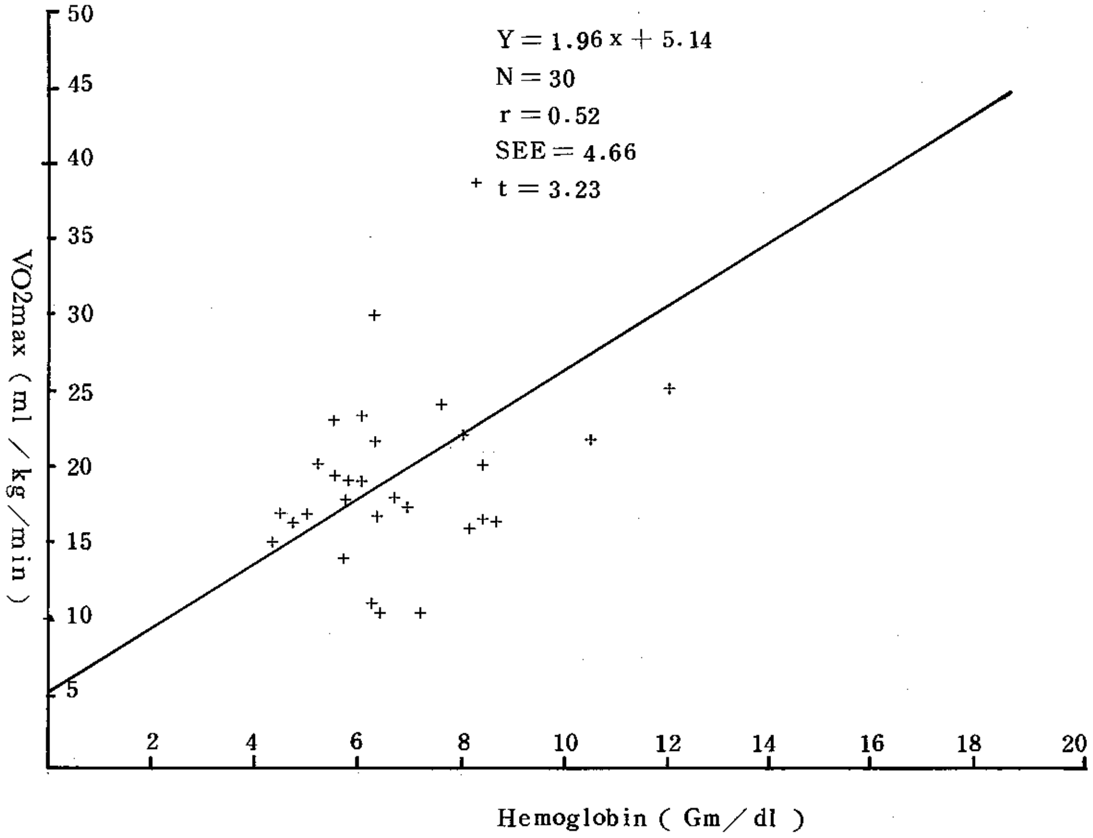

圖 2　尿毒症患者單位體重最大攝氧量與血液中血紅素之濃度（gm／dL）成綫性正相關。（$P < 0.05$）

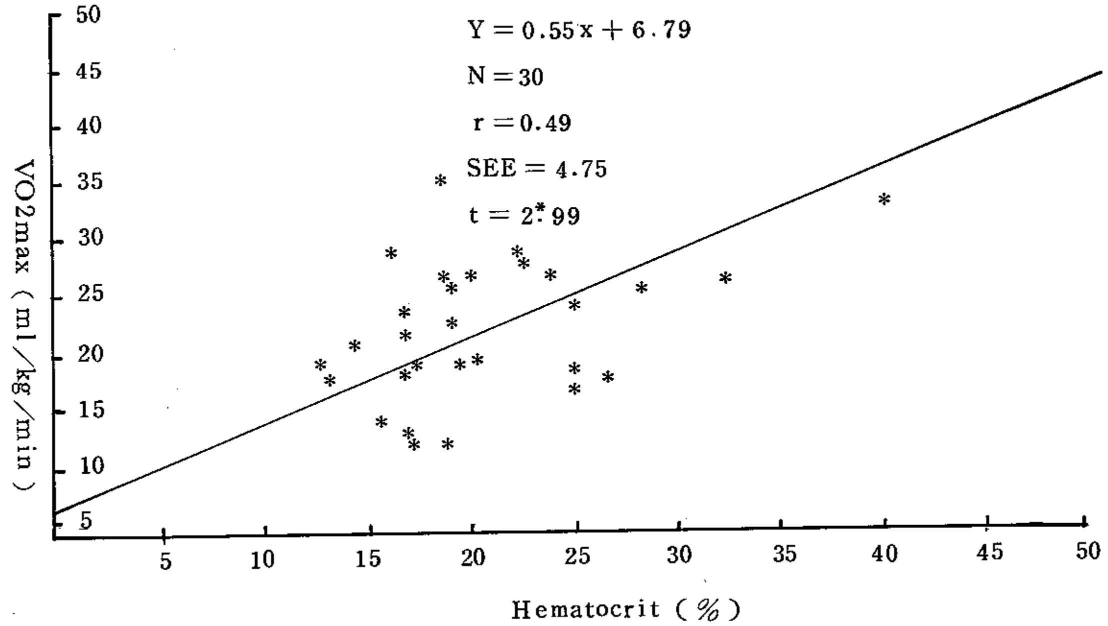

圖 3 尿毒症患者單位體重最大攝氧量與血比容成綫性正相關。(P < 0.05)

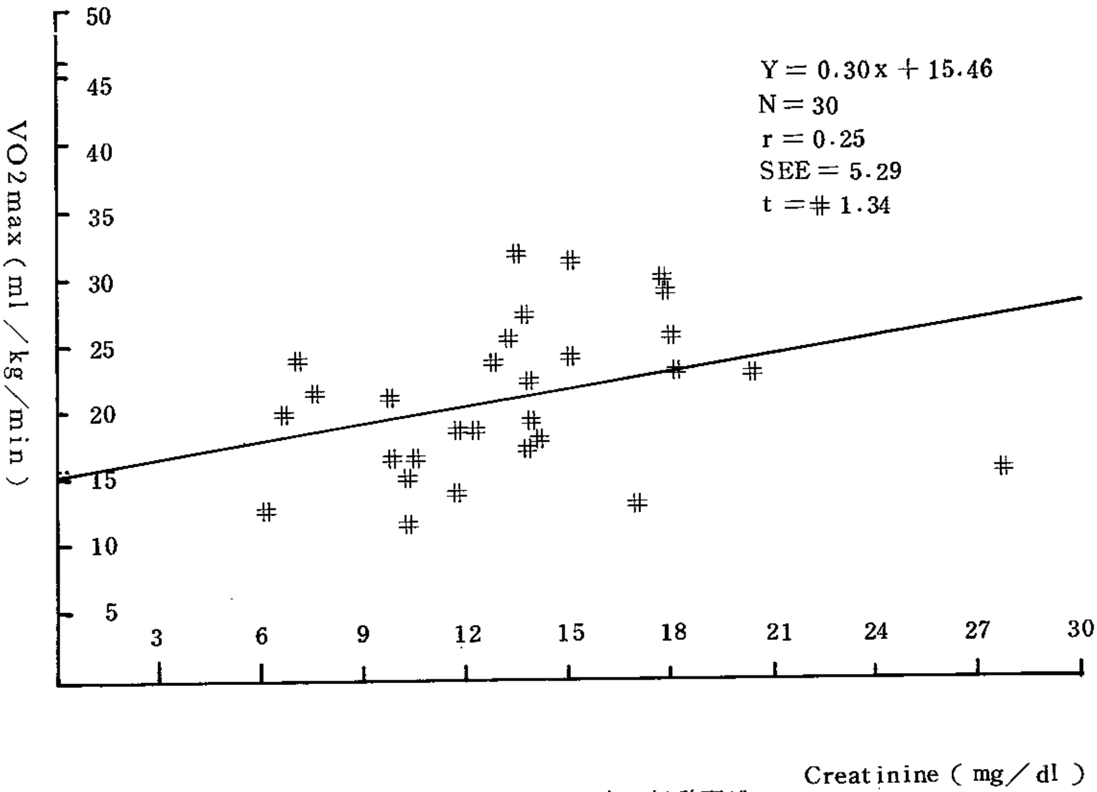

圖 4 尿毒症患者單位體重最大攝氧量與血液肌氨酸酐濃度無顯著綫性相關。(P > 0.1)

CARDIOPULMONARY FUNCTION IN THE LONG TERM HEMODIALYSIS PATIENTS DURING BICYCLE EXERCISE

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Long term hemodialysis of uremic patients can keep on their living, but they still have many problems like severe anemia, atherosclerosis, and decreasing physical fitness, etc.

In this report, a symptomatic maximum bicycle exercise test was given to 19 male and 11 female uremic patients who were in stable condition. This test was administered some 18-36 hours after hemodialysis. The patients experienced a progressive increase of resistance on the bicycle until the patient couldn't tolerate it. During exercise, oxygen uptake (VO2), pulmonary ventilation (VE), respiratory exchange ratio (R) and heart rate (HR) were measured breath-by-breath with a MGC-2000 system and lactate level was determined by the enzymatic method in the venous blood sampled 5 minutes after maximal exercise. The results were compared with the data of 43 male and 19 female healthy adults who had similar physical characteristics.

The mean values (±S.D.) of maximum O2 consumption per Kg body weight in male & female uremic patients were 21.4 (±5.5) and 16.0(±2.8) ml/Kg/min, which were significantly lower than those respective values in normal males and females (48.3 ± 7.9 & 29.9 ± 4.3ml/Kg/min). This was due to the decrease in the maximum heart rate and maximum O2 pulse.

The cause of decreased maximal heart rate in uremic patients may be due to the dysfunction of the sympathetic nervous system. Also the abnormal lower O2 pulse may be due to anemia & the decreases in myocardial contractility & oxygen extraction in skeletal muscle.

In each case the uremic patients achieved a near normal respiratory exchange ratio which indicated that they had worked up to their maximum physical capacity. But they still had a marked decrease in physical fitness. So, how to improve the physical fitness of uremic patient is worthy of further study.

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THE EXCITABILITY OF SPINAL MOTONEURONS IN STROKE PATIENTS

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Thirty hemiplegics and 15 normal persons were enrolled in this study. Measuring the recovery time of H reflex by dual stimulation technique to tibial nerve was performed to evaluate the excitability of spinal motoneurons. It was found that the recovery time of H reflex in normal persons and non-hemiplegic sides of hemiplegics was 57.0 ± 27.3 msec and 57.3 ± 21.4 msec respectively. The recovery time of hemiplegic sides was 37.5 ± 12.8 msec and it was very significantly shorter than the normal ones. The shortening of the recovery time showed good correlation with the neurological recovery as well as the spasticity of the patients. These findings approved that with higher frequency of dual stimulation the recovery time of H reflex is an useful index in the clinical evaluation of spinal motoneuron excitability.

Key words: stroke, H reflex, spinal motoneuron excitability

INTRODUCTION:

The H reflex, introduced by Hoffmann in 1918, is accepted as a monosynaptic spinal reflex. The afferent is Ia sensory fiber and the efferent is the alpha motor neuron. Since it bypasses the muscle proprioceptors, it can give a more direct measure of spinal motoneuron excitability than the mechanically evoked stretch reflex. In early 1950s, Magladery and associates found that when the afferent nerve stimilus used to elicit the H reflex was preceded at varying intervals by a conditioning shock, the amplitude of the test H reflex was affected.[3] They noted that patients with any type of UMN lesions had H recovery curves with earlier recovery, more complete recovery, and less late depression than had normal persons.

The present study employed the same technique as that of Magladery, but focused on the refreactory period of the H reflex after dual stimulations. The purposes of this study were to find out normal refractory period of H reflex in our laboratory and to evaluate the spinal motoneuron excitability in hemiplegic patients.

MATERIALS AND METHODS

Thirty hemiplegics were collected from the Department of Physical Medicine and Rehabilitation of National Taiwan University Hospital. Among them 12 were females and 18 were males. Their age ranged from 30 to 78 years with an average of 60.8 years. Fourteen cases were right hemiplegic and 16 cases were left hemiplegic as the result of CVA. No case had accompanied low back pain. The neurological deficits ranked from hemiparesis to hemiplegia. The interval between onset of CVA and study was 10 days to 4 years, the mean duration was 9.9 months.

Fifteen normal persons, 10 females and 5 males, were chosen as the control group. Their age ranged from 47 to 71 years, with an average of 54.1 years. Neither of them had any systemic disease, nor back and leg pain.

The study was done in a quiet room. The room temperature was kept around 20 – 25°C. A complete neurological examination was performed in each case, which included the deep tendon reflex and spasticity. The motor function of hemiplegics was evaluated according to Brunnstrom's classification (stage I–VI).[2] The subject was put in a prone position with the feet hanging over the edge of the bed. Both knees were extended and the ankles were kept at neutral position.

The H reflex was studied by a Medelec MS-6 electromyographic machine using surface electrodes. The stimulating electrode was put alone the course of the tibial nerve in the midpopliteal fossa. The cathode was placed proximal to the anode. The active electrode was put on the muscle belly of medial gastrocnemius muscle, 12 cm below popliteal crease, and the reference electrode was distal to the active one. A single stimulation with 0.2 msec duration and 75-150V voltage was first applied to get a maximal H reflex. Then dual stimulations were applied with the same duration and voltage. The frequency of dual stimulation was one per second. There were two successive H reflexes elicited after the two successive stimulations. (Figure 1) The interval between these two stimulations was decreased from 130 msec gradually till the second H reflex completely diminished. The least adjustable interval was 20 msec in our MS-6 EMG machine. The first H reflex was named conditioning H reflex and the second one was test H reflex, following that by

Olsen.[5] During the moment, that interval was designeated as the recovery time of H reflex.

The hemiplegic patients were classified into two groups. Those who had motor function above Brunnstrom stage IV were defined as good motor group and those who did not reach stage IV as poor motor group.

RESULTS

The recovery time of H reflex in normal controls and hemiplegics were shown in table 1. In control group, the recovery time ranged from 25 to 110 msec, with a mean of 57.0 msec. There was no significant difference between right sides (56.7 ± 27.0 msec) and left sides (57.3 ± 28.6 msec). In study group, the recovery time of hemiplegic sides ranged from 20 to 60 msec, and that of non-hemiplegic sides ranged from 30 to 120 msec. The mean recovery time of hemiplegic sides was 37.5 msec, and that of non-hemiplegic sides was 57.3 msec. The recovery time of H reflex of hemiplegic sides was very significantly shorter than that of non-hemiplegic sides and that of normal controls ($P<0.0005$).

The difference of the recovery time of H reflex between both sides in control group was 0 to 20 msec and it was nearly equal between both sides. (Figure 2) In study group, the recovery time of both sides was not equal. (Figure 3) The difference of the recovery time between non-hemiplegic and hemiplegic sides was −5 to 85 msec and the former was usually longer than the latter.

Table 2 shows that the recovery time of H reflex in good motor group (42.0 ± 12.1 msec) was significantly longer than that in poor motor group (33.0 ± 12.4 msec) ($P<0.025$).

As regard to the severity of spasticity, it showed that the recovery time of patients with spasticity (32.5 ± 10.5 msec) was significantly shorter than that of patients without spasticity (41.9 ± 13.4 msec) ($P< 0.025$). (Table 3)

DISCUSSI

Several studies had utilized the H reflex recovery curve after dual stimulation to evaluate the excitability of spinal motoneurons in normal persons and patients with spasticity and rigidity.[3-6] As shown in figure 4, normal subjects showed "early facilitation" about 8 msec after a liminal afferent conditioning volley. The H reflex amplitude then gradually decreased as the stimulation interval was increased to 20 msec. From 20 msec to approximately 100 msec there was a complete inhibition of the H reflex called "early depression". As the stimulation interval was further extended, there was gradual recovery of the H reflex amplitude. This recovery was followed by a stage of "late depression" at stimulation intervals of 400 to 800 msec. After a stronger conditioning volley, the H reflex recovery curve showed no early facilitation, the recovery from early depression was delayed and the overall recovery of the curve was reduced. In patients with any type of upper motor neuron lesion, the H reflex recovery curve had earlier recovery, more complete recovery, and less late depression than that of normal persons.[3] The main clinical drawback of this method is that considerable time is required to measure the H amplitude and plot the curve. This study also employed the dual stimulation technique with maximal H reflex but only the recovery time of test H reflex was recorded. The recorded recovery time is defined as the refractory period of S-1 motoneurons, and we presumed that physiologically it represents the excitability of the motoneurons.

The physiological aspects of the refractory period of H reflex are complex and remain unsolved. A number of factors have been proposed.[1] Renshaw cell inhibition of the alpha motoneurons could account for the first 5 to 15 msec of this period. Later in this period. Ib fibers carrying impulses from the Golgi tendon organs would further depress the alpha motoneurons. The other factor might be the reduction of the facilitory Ia impulses to the alpha motoneurons because of the unloading of the muscle spindle by the muscle twitch.

In previous reports, the recovery time of H reflex was not a good indicator of the excitability of spinal motoneuron. It was only a parameter in the recovery curve of H reflex because the difference of the recovery time of H reflex between normal persons and patients with UMN lesions was variable. Olsen et al reported that the recovery time of H reflex in normals and patients was identical (30 ± 3 msec).[5] The result of Miglietta's study showed that the recovery time of H reflex in normals and either side of hemiplegics was 40 msec.[4] On the contrary, Yap noted that there was a shift of the recovery point to the left of the normal group (63 ± 13 msec) for the pyramidal group (40 ± 17 msec).[6] The major difference of technique between these two groups of studies is that the frequency of dual stimulation of the former group was less than 6 per minute and that of the latter group was more than 6 per minute. The higher the frequency is given, the more suppression effect is shown on H reflex. The frequency of dual stimulation in the study was 60 per minute. The results showed that the recovery time of normal controls and non-hemiplegic sides of hemiplegics was identical and it was very significantly longer than that of the hemiplegic sides. So the difference of the recovery time of H relfex between normals and patients will become more apparent under higher frequency of dual stimulation.

There was good equality between both sides of normal controls no mater what the value of the recovery time was. The equality was lost in hemiplegics and the recovery time of non-hemiplegic sides was usually longer than hemiplegic sides. This phenomenon indicated that there is parallel relationship between the recovery time of H reflex and the change of spinal motoneuron excitability.

In the studies of Olsen et al[5] and Yap[6], the patients with spasticity were regarded as the group of upper motor neuron lesion involving the pyramidal tract. By employing dual stimulation with maximal H reflex, Olsen et al found that in spasticity the increase in excitability was the same whether this was severe or mild.[5] In this study, the presence of spasticity represented a more severe stroke. By applying higher frequency of dual stimulation, the shortening of the recovery time of H reflex showed good correlation with the neurological recovery and the spasticity of the patients. However, due to the small sampling size, the linear relationship between the recovery time of H reflex and the severity of stroke (Brunnstrom stage I–VI and spasticity ±~ ++++) was not established yet.

The results of this study approved that with higher frequency of dual stimulation, the recovery time of H reflex is an useful index in the clinical evaluation of spinal motoneuron excitability.

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Table 1. The recovery time of H reflex in hemiplegics and normal controls

	No.	Range (msec)	Mean ± SD (msec)
Control group	30	25–110	57.0 ± 27.3 a
Right side	15	25–110	56.7 ± 27.0 b
Left side	15	25–110	57.3 ± 28.6 c
Study group			
Normal side	30	30–120	57.3 ± 21.4 d
Hemiplegic side	30	20–60	37.5 ± 12.9 e

Paired t-test: b vs c, NS; d vs e, $p < 0.0005$

Student's t-test: a vs d, NS; a vs e, $P < 0.0005$

Table 2. The relationship between the recovery time of H reflex and the neurological recovery of hemiplegics

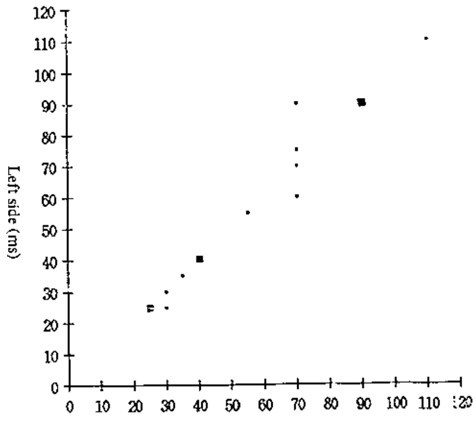
	Good motor group N = 15	Poor motor group N = 15	
Recovery time	42.0 ± 12.1 msec	33.0 ± 12.4 msec	$P < 0.025$

Student's t-test

Table 3. The relationship between the recovery time of H reflex and spasticity

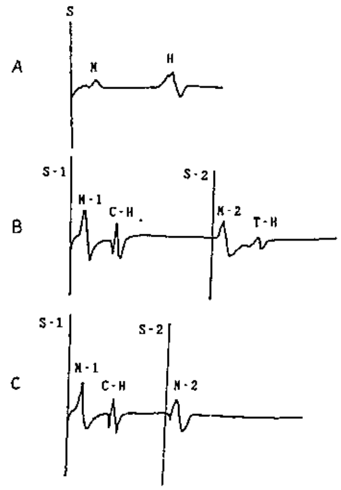
	No	Recovery time	
Spasticity (+)	14	32.5 ± 10.5 msec	
Spasticity (−)	16	41.9 ± 13.4 msec	P < 0.025

Student's t-test



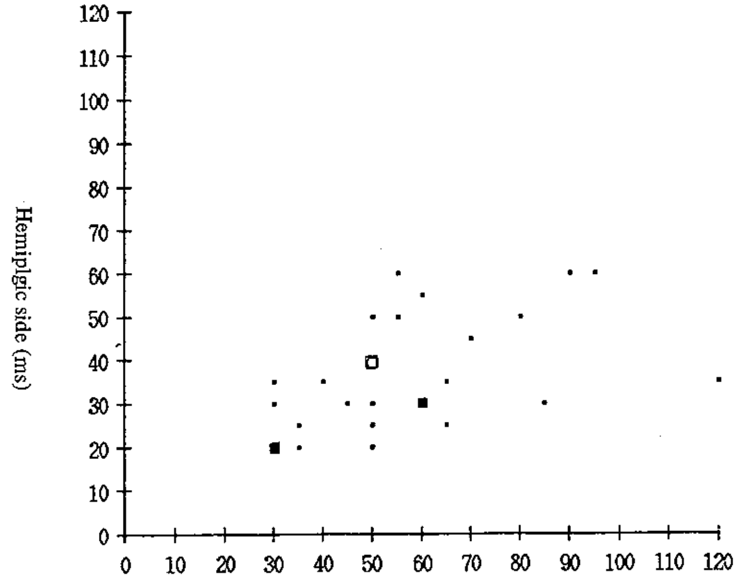
: one set of data; : two sets of data

Figure 2. Symmetrical distribution of the recovery time of H reflex of both sides in normal controls



C-H: Conditioning H-reflex T-H: Testing H-reflex

Figure 1. A) The maximal H reflex. B) Application of dual stimulation. C) When the test H reflex diminishs the interval between S1 and S2 is the recovery time of H reflex.



non-hemiplegic side (ms)

: one set of data; : two sets of data; : three sets of data

Figure 3. Asymmetrical distribution of the recovery time of H reflex of both sides of hemiplegics. A tendency of Shifting to non-hemiplegic side was noted.

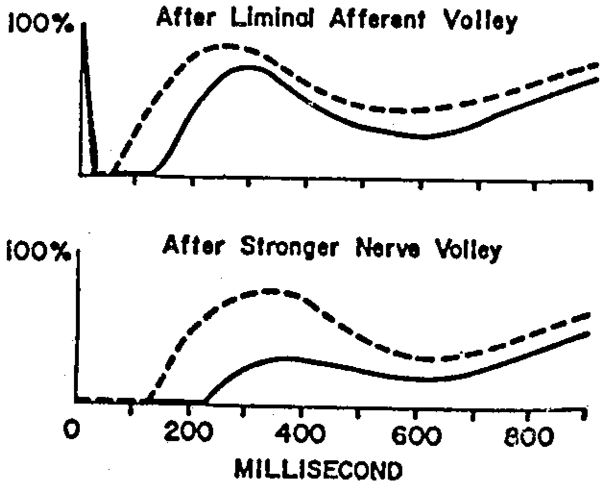


Figure 4. H recovery curve after a conditioning volley in patients with upper motor neuron lesions and in normals. (Dotted line represents the patients with upper motor nuron lesions.) (From Magladery and associates.[3])