

Original Article

Vascular Responses to Acupuncture at the Kidney *Jeonggyeok* in Diabetic and Normal Groups Assessed by the Second Derivative of the Finger Photoplethysmogram Waveform

Youn In-yae*, Kim Ji-na*, Lee Ji-su*, Moon Sung-il*,
Kim Jin-yi** and Jeong Si-yeong***

*Dept. of Acupuncture and Moxibustion, National Medical Center

**Dept. of Oriental Neuropsychiatry, National Medical Center

***Dept. of Acupuncture and Moxibustion, Je-in Hospital of Oriental Medicine

국문초록

가속도맥파로 평가한 당뇨군과 정상군의 신정격 자침으로 인한 혈관변화

윤인애* · 김지나* · 이지수* · 문성일* · 김진이** · 정시영***

*국립중앙의료원 침구과

**국립중앙의료원 신경정신과

***제인한방병원 침구과

목적 : 신정격 자침이 당뇨군과 정상군의 혈관변화에 미치는 영향을 알아보기 위해 가속도맥파를 이용한 실험을 설계하였다.

방법 : 20명의 당뇨군과 20명의 정상군에서 신정격 자침 이전과 이후, 2회에 걸쳐서 Cardio Peri SA6000을 이용하여 가속도맥파를 측정하였다. 가속도맥파의 b/a, c/a, d/a 및 연령지수를 통해 혈관상태를 평가하였다.

결과 : 1. 당뇨군과 정상군의 신정격 자침 이전 가속도맥파 측정에서 당뇨군이 정상군보다 b/a값($p=0.000$), 연령지수(AI)($p=0.000$)는 유의하게 높았으며, c/a값($p=0.000$), d/a값($p=0.000$)은 유의하게 낮았다.

2. 당뇨군에서 신정격 자침 이후 가속도맥파의 b/a값($p=0.004$), 연령지수($p=0.012$)는 유의하게 낮아졌으며, c/a값($p=0.026$)은 유의하게 높아졌다.

· Acceptance : 2011. 1. 21. · Adjustment : 2011. 2. 1. · Adoption : 2011. 2. 7.

· Corresponding author : Youn In-yae, Dept. Acupuncture & Moxibustion, National Medical Center, Eulji-ro 6ga, Chung-gu, Seoul, 100-799 Republic of Korea
Tel. 82-2-2260-7454 E-mail : eknowkey@hanmail.net

3. 정상군에서 신경적 자침 이후 가속도맥파의 b/a값($p=0.025$)은 유의하게 낮아졌다.

결론 : 신경적 자침이 당뇨로 인해 유발된 혈관의 탄력도 감소 및 노화를 다소 회복시킬 수 있는 것으로 사료된다.

핵심 단어 : 가속도맥파, 당뇨, 침, 신경적

I. Introduction

Recently, the prevalence rate of diabetes mellitus (DM) in Korea has been increasing rapidly due to high growth of economy and changes in dietary lifestyle. Vascular complication is one of diabetic complications which have frequently occurred by obesity, hyperglycemia and impaired glucose metabolism¹⁾.

The second derivative of the finger photoplethysmogram(SDPTG) waveform permits the assessment of peripheral circulation and changes elicited by vasoactive agents by detailed analysis of digital volume pulse(DVP) analysis²⁾. In particular, SDPTG allows more accurate recognition of the circulation phases, and it is easier to interpret than the DVP waveform. The SDPTG consists of 5 waves and each wave is consecutively named 'a', 'b', 'c', 'd', and 'e' wave, respectively. The 'a' and 'b' waves are included in the early systolic phase and the 'c' and 'd' waves in the late systolic phase of the photoplethysmogram(PTG)(Fig. 1). Epidemiologic studies have shown that the information extracted from the SDPTG waveform reflects both the elasticity of the aorta and peripheral arteries^{3,4)}, and that it is associated closely with age^{2,5)}, hypertension⁶⁾, DM⁵⁾, atherosclerosis^{3,4)} and end-stage renal disease⁷⁾.

Acupuncture has been used for the treatment of DM and related complications during the past several decades. It is known to be effective not only in treating DM, but also in preventing and managing complications of the disease⁸⁾. The effects of acupuncture on DM have been observed experimentally and clinically⁹⁻¹⁴⁾.

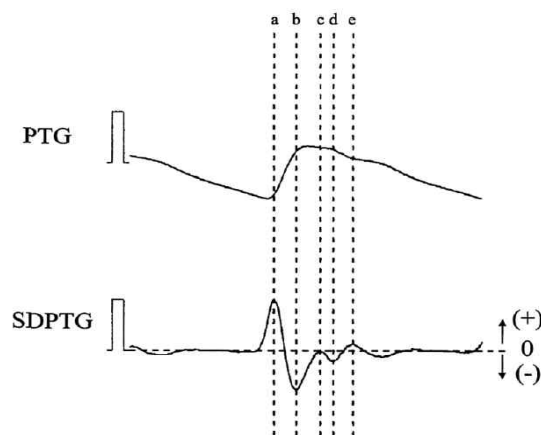


Fig. 1. A schema of the finger photoplethysmogram(PTG) and the second derivative of the finger photoplethysmogram(SDPTG)

The SDPTG consists of 5 waves and each wave is consecutively named 'a', 'b', 'c', 'd', and 'e' wave, respectively. The 'a' and 'b' waves are included in the early systolic phase and the 'c' and 'd' waves in the late systolic phase of the PTG

We tonify the LU₈(*Jingqu*) and the KI₇(*Fuliu*) acupoint and sedate the SP₃(*Taibai*) and the KI₃(*Taixi*) acupoint. That is the way to treat the deficiency of the Kidney system in *Sa-Ahm* acupuncture and is called as Kidney *Jeonggyeok*¹⁵⁾. A previous study showed that many oriental doctors in the past considered deficiency of the kidney system as the etiology of DM(called 消渴 in oriental medicine)¹⁰⁾. Especially Joo insisted the deficiency of the Kidney-yin(腎陰不足) is the main reason for DM¹⁶⁾. We hoped, if we make improvement on diabetic patients by acupuncture, a decrease of arteries distensibility due to DM could be improved too.

Although there were many studies done on acupuncture effect in DM⁹⁻¹⁴⁾, there was not any study done on vascular changes to acupuncture

treatment in diabetic patients by the SDPTG waveform. Therefore, in this study, we tried to evaluate the vascular changes in diabetic patient before and after acupuncture treatment on Kidney *Jeonggyeok* by using the SDPTG waveform.

II. Subjects, Materials and Methods

A. Period

This study was proceeded for four months, from August to December, 2010.

B. Subjects

Healthy volunteers were recruited from the local community around our medical center by advertisement.

Diabetic patients were those who were diagnosed with DM at endocrinology in National Medical Center.

The elasticity and stiffness of the aorta and peripheral arteries are strongly related to age^{2,5)}, we tried to match age of both groups.

The subjects were studied fasting, having abstained from caffeine, alcohol or smoking for 12 hours. The study was not approved by the clinical research ethics committee because our medical center doesn't have one, but all the subjects gave written, informed consent.

C. Materials

1. Needle

The stainless steel needles which are 30mm long and 0.3mm in diameter(Dongbang Acupuncture, Incorporation) were used.

2. Measuring device for the SDPTG waveform

Cardio Peri SA6000 was used

D. Methods

All recordings were made in a quiet laboratory with a temperature of $24^{\circ}\text{C}\pm 1^{\circ}\text{C}$. All subjects were allowed to rest and to acclimatize for at least 30 minutes before recordings commenced.

1. The measurement of the SDPTG waveform before the acupuncture

The measurements were performed for 3 minutes with each subject in supine position. They were not allowed to make any sound or movement. A PTG transmitting infrared light placed on the index finger of the right hand was used to obtain the DVP. The SDPTG indices were automatically obtained by the device.

2. Acupuncture treatment

After the measurement of the SDPTG waveform, the subjects were treated with acupuncture for 15 minutes. We firstly tonify the LU₈(*Jingqu*) and the KI₇(*Fuliu*) acupoint and secondly sedate the SP₃(*Taibai*) and the KI₃(*Taixi*) acupoint on left side in male subjects and right side in female subjects. The acupuncturist did the therapeutic method such as respiratory, rotational and directional methods for tonification and sedation. That is the way of treating the deficiency of the Kidney system in *Sa-Ahm* acupuncture and is called as Kidney *Jeonggyeok*¹⁵⁾. The textbook of acupuncture and moxibustion(鍼灸學) was used for the standardization for locating the point.

3. The remeasurement of the SDPTG waveform after the acupuncture

The remeasurements were performed in the same condition as before the acupuncture.

4. The SDPTG waveform indices

Typically, the SDPTG waveform comprises five distinct waves: a to e. To describe these SDPTG components quantitatively, the height of each wave was measured from the baseline, the values above

the baseline being positive and those under it negative and was termed a to e¹⁷⁾. The ratio of b to a, c to a, and d to a was calculated automatically. The SDPTG aging index(AI), defined as(b-c-d-e)/a according to a previous study by Takazawa et al²⁾, was also calculated automatically.

E. Statistical analysis

Data were expressed as mean±standard deviation. The paired *t*-test was used for comparison between pre- and post-acupuncture periods in both groups. The independent *t*-test was used for comparison between diabetic group and normal group in pre-acupuncture period. A *p* value of < 0.05 was considered significant. All statistical analyses were performed with SPSS 12.0K for Windows software.

III. Results

A. Characteristics of the subjects

The study group comprised 20 (12 female) healthy subjects, 20 (13 female) diabetic patients (refer to Table 1 for the mean age and standard deviation). There were no significant differences between the two subject groups for either gender (Table 1).

In normal group, none had cardiac disease, endocrinological disease or were taking any medications.

In diabetic group, their fasting glucose level were above 120mg/dL and were diagnosed as type 2 diabetes. They were all under diabetic medications and none were injecting insulin. The mean

Table 1. Distribution of Age and Gender

Group		Normal group (n=20)	Diabetic group (n=20)
Age(mean±SD)		57.9±2.8	60.5±3.0
Gender	Female	12(60%)	13(65%)
	Male	8(40%)	7(35%)

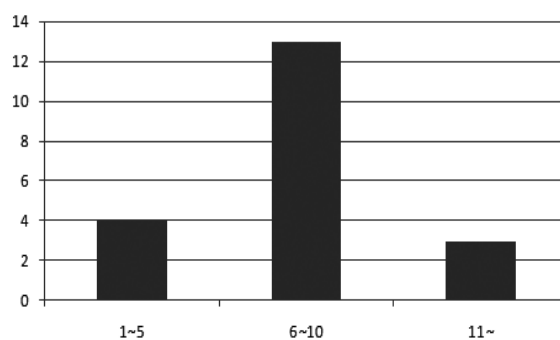


Fig. 2. The duration of disease

and standard deviation of the duration of disease is 7.4±2.30.(Fig. 2)

2. Comparison of indices of SDPTG between DM group and normal group in the pre-acupuncture period

The SDPTG indices before acupuncture between two groups are shown in Table 2. Comparing both indices, b/a, c/a, d/a and SDPTG AI all showed significant differences (Table 2).

Table 2. Comparison of Indices of SDPTG between DM Group and Normal group in the Pre-acupuncture Period[†]

	DM group	Normal group	<i>p</i> -value
b/a	-0.33±0.24	-0.73±0.14	0.000 [†]
c/a	-0.23±0.16	0.02±0.10	0.000 [†]
d/a	-0.37±0.16	-0.13±0.12	0.000 [†]
b-c-d-e/a (SDPTG AI)	-0.36±0.17	-0.72±0.24	0.000 [†]

Data are presented as mean ± standard deviation; [†] significantly different between two groups, *p*<0.05; SDPTG AI= second derivative of the finger photoplethysmogram aging index, defined as (b . c . d . e)/a; b/a=the ratio of the absolute value for the height of the *b* wave to that of the *a* wave; c/a=the ratio of the absolute value for the height of the *c* wave to that of the *a* wave; d/a=the ratio of the absolute value for the height of the *d* wave to *a* wave.

C. Comparison of indices of SDPTG in DM group in the pre- vs. post-acupuncture periods

The SDPTG indices before and its changes after

acupuncture in DM group are shown in Table 3. Comparing pre- vs. post-acupuncture periods, b/a and SDPTG AI decreased significantly and c/a increased significantly among this group. Otherwise d/a increased but was not significant (Table 3).

Table 3. Comparison of Indices of SDPTG in DM Group in the Pre- vs. Post-acupuncture Periods

	Pre-acupuncture	Post-acupuncture	p-value
b/a	-0.33±0.24	-0.50±0.13	0.004 [†]
c/a	-0.23±0.16	-0.18±0.15	0.026 [†]
d/a	-0.37±0.16	-0.34±0.18	0.129
b-c-d-e/a (SDPTG AI)	-0.36±0.17	-0.51±0.29	0.012 [†]

Data are presented as mean ± standard deviation; [†] significantly different from pre-acupuncture values, $p < 0.05$; SDPTG AI=second derivative of the finger photoplethysmogram aging index, defined as $(b \cdot c \cdot d \cdot e)/a$; b/a =the ratio of the absolute value for the height of the b wave to that of the a wave; c/a=the ratio of the absolute value for the height of the c wave to that of the a wave; d/a=the ratio of the absolute value for the height of the d wave to a wave.

D. Comparison of indices of SDPTG in normal group in the pre- vs. post- acupuncture periods

The SDPTG indices before and its changes after

Table 4. Comparison of Indices of SDPTG in Normal Group in the Pre- vs. Post-acupuncture Periods

	Pre-acupuncture	Post-acupuncture	p-value
b/a	-0.73±0.14	-0.78±0.41	0.025 [†]
c/a	0.02±0.10	0.22±0.10	0.453
d/a	-0.13±0.12	-0.13±0.10	0.414
b-c-d-e/a (SDPTG AI)	-0.72±0.24	-0.72±0.30	0.487

Data are presented as mean±standard deviation; [†] significantly different from pre-acupuncture values, $p < 0.05$; SDPTG AI=second derivative of the finger photoplethysmogram aging index, defined as $(b \cdot c \cdot d \cdot e)/a$; b/a=the ratio of the absolute value for the height of the b wave to that of the a wave; c/a=the ratio of the absolute value for the height of the c wave to that of the a wave; d/a=the ratio of the absolute value for the height of the d wave to a wave.

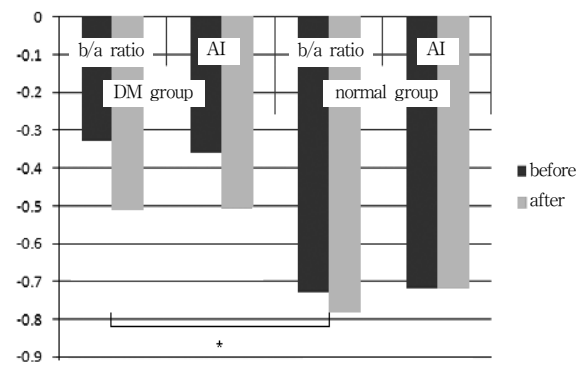


Fig. 3. Mean change of b/a ratio and the SDPTG AI. The SDPTG AI was defined as $(b-c-d-e)/a$. There were significant differences of b/a ratio in both groups and the SDPTG AI in DM group between pre- and post-acupuncture at the Kidney *Jeonggyeok*. * : $p < 0.05$.

acupuncture in normal group are shown in Table 4. Comparing pre- vs. post-acupuncture periods, c/a and d/a and SDPTG AI did not show significant differences among normal group. Otherwise, b/a decreased significantly in this group (Table 4, Fig. 3).

IV. Discussion

PTG is a simple and low-cost optical technique that can be used to detect blood volume changes in the microvascular bed of tissue. It is often used non-invasively to make measurements at the skin surface¹⁸. The fingertip PTG expresses changes in the volume of blood in the fingertip as pulse waves, providing information on beats of aortic origin, characteristics of the vascular system, properties of peripheral vessels, and the state of blood flow. The SDPTG is a convenient and objective technique of analyzing PTG waves. The SDPTG consists of the initial positive wave(a wave), early negative wave (b wave), re-upsloping wave(c wave), late re-downsloping wave(d wave), and diastolic positive wave(e wave) and the shift from the baseline to the peak of each wave is taken as the value for each wave¹⁹.

Several investigators have studied the physiological meanings and clinical implications of the

SDPTG waveform. The b/a ratio consists of waves in the early systolic phase, which are pressure waves mainly caused by the first vascular response to blood ejection from the left ventricle. Thus, it reflects change in the phase that most expresses the elasticity of the arteries¹⁹⁾. The b/a ratio and The SDPTG age index(AI)(b-c-d-e)/a have been reported to increase with age^{2,19,20)}, disease of diabetes mellitus²¹⁾, coronary arteries²²⁾ and also in smokers²³⁾. The c/a ratio is known to decrease with aging in adults. This change is considered to be associated with the d wave decrease due to aging but the implication of the c wave is unknown¹⁹⁾. The d/a ratio increases because of functional vascular wall tension arising from the elevated intravascular pressure and organic vascular wall sclerosis due to arteriosclerosis. It decreased with aging and increasing systolic blood pressure^{2,22,24)}.

DM is a serious chronic metabolic disorder that has a significant impact on the health, quality of life, and life expectancy of patients, as well as on the health care system²⁵⁾. It is expected that by 2020, the number of diabetic patients will be almost 250 million world wide²⁶⁾. Several arterial changes have been described with diabetic patients. Kim SW et al reported that arterial stiffness of diabetic patients are worse than normal people²¹⁾. Kim KJ et al reported longer duration of DM could be a predictors of increased arterial stiffness in type 2 DM patients²⁷⁾. Izuhara M et al reported that the severity of carotid arteriosclerosis and the aortic stiffness parameters were significantly correlated with arteriosclerotic risk factors such as age, sex and DM²⁸⁾. The microvascular and macrovascular complications related DM increase as the duration of DM increases. It is reported that the type 2 DM patients have risk of getting cardiovascular diseases 2 to 4 times higher than normal people^{29,30)}.

Acupuncture has been used for the treatment of DM and related complications during the past several decades. Acupuncture may be effective in treating not only diabetes, but also in preventing and managing complications of the disease⁸⁾. The effects of acupuncture on diabetes have been obser-

ved experimentally and clinically. Animal experiments have shown that electroacupuncture improves insulin sensitivity in diabetic mice^{12,13)}. Other methods have also been employed such as point injections with different kinds of oriental herbal medicine extracts also help to decrease the levels of serum glucose^{11,14)}.

In this study, among many acupuncture methods, we decided to apply Kidney *Jeonggyeok* which is a way to treat deficiency of the Kidney system in *Sa-Ahm* acupuncture¹⁵⁾. DM is called as *So-gal*(消渴) in oriental medicine. Many oriental medical doctors presented different etiologies for *So-gal*. Deficiency of the Kidney system is one of them and is considered to be an important theory¹⁰⁾. Based on this theory, some studies showed significant improvement in treating DM using BL₂₃ (*Shenshu*) acupoint^{10,11,14)}.

Sa-Ahm's acupuncture treatment consists of deficiency/excess treatments and coldness/heat treatments in which Five-*Shu*(Five-Transporting or 5-*Shu*) points are used according to tonification and sedation. This principle is based on creation and control cycles of the Five Element theory, as well as *Nanjing's* theories presented in the 50th and 69th issues. In Kidney *Jeonggyeok*, we firstly tonify the LU₈(*Jingqu*) and the KI₇(*Fuliu*) acupoint and secondly sedate the SP₃(*Taibai*) and the KI₃(*Taixi*) acupoint¹⁵⁾.

The aim of this study was, by using the SDPTG, to compare the vascular state between DM group and normal group and see whether acupuncture in Kidney *Jeonggyeok* can make vascular changes.

The salient findings of this study were that, in DM group, b/a ratio and AI indices were higher than normal group, whereas c/a and d/a ratio indices were lower than normal group. And in DM group, b/a, c/a ratio and AI indices were improved with manual acupuncture in Kidney *Jeonggyeok*, whereas in normal group, only b/a was improved. The improvement of the b/a, c/a ratio AI indices with acupuncture in Kidney *Jeonggyeok* suggested that DM patients had a decrease of arteries distensibility, which could be partially reverted with

acupuncture.

There are some limitations concerning this study. First, there were only 20 subjects in each group. It could be done to large number of subjects to get more accurate results. Second, the SDPTG indices were measured just once after the acupuncture. The follow ups after certain periods of time are needed.

In conclusion, this study demonstrated an acute effect of manual acupuncture in Kidney *Jeonggyeok* on SDPGT indices in DM group. We believe that this can be attributed to the therapeutic effect of Kidney *Jeonggyeok* on DM. These results emphasize the importance of employing acupuncture in basic and clinical studies on stiffness and aging of vascular beds related to DM.

V. Conclusion

We tried to compare vascular state between DM group and normal group by using the SDPTG, and see acupuncture(Kidney *Jeonggyeok*) effect on vascular change in both group. The results were as follows.

1. The SDPTG indices differences between DM group and normal group were significant.
2. After acupuncture at Kidney *Jeonggyeok*, b/a, c/a and AI in DM group were improved significantly.
3. After acupuncture at Kidney *Jeonggyeok*, only b/a in normal group was improved significantly.

VI. References

1. Korean diabetes association. Text book of diabetes. 2nd Ed. Korea medical book publisher. 1998 : 1-569.
2. Takazawa K, Tanaka N, Fujita M, Matsuoka O, Saiki T, Aikawa M et al. Assessment of vasoactive agents and vascular aging by the second derivative of photoplethysmogram waveform. Hypertension. 1998 ; 32 : 365-70.
3. Bortolotto LA, Blacher J, Kondo T, Takazawa K, Safar ME. Assessment of vascular aging and atherosclerosis in hypertensive subjects: second derivative of photoplethysmogram versus pulse wave velocity. Am J Hypertension. 2000 ; 13 : 165-71.
4. Miyai N, Miyashita K, Arita M, Morioka I, Kamiya K, Takeda S. Noninvasive assessment of arterial distensibility in adolescents using the second derivative of photoplethysmogram waveform. Eur J Appl Physiol. 2001 ; 86 : 119-24.
5. Nichols WW, O'Rourke MF. Properties of the arterial wall, in McDonald's blood flow in arteries: theoretical, experimental and clinical principles, 3rd Ed. London : Edward Arnold. 1990 : 77-114.
6. Safar ME, Frohlich ED. The arterial system in hypertension: a prospective view. Hypertension. 1995 ; 26 : 10-4.
7. London GM, Gue'rin AP, Marchais SJ, Pannier B, Safar ME, Day M, Metivier F. Cardiac and arterial interactions in end-stage renal disease. Kidney Int. 1996 ; 50 : 600-8.
8. Hu H. A review of treatment of diabetes by acupuncture during the past forty years. J Tradit Chin Med. 1995 ; 15 : 145-54.
9. Liao H, Xi P, Chen Q, Yi L, Zhao Y. Clinical study on acupuncture, moxibustion, acupuncture plus moxibustion at Weiwanshiashu(EX-B3) for treatment of diabetes. Chinese Acupuncture and moxibustion. 2007 ; 27(7) : 482-4.
10. Moon JH, Park SG, Kwon EH, Song KK, Jeon KO, Shin HC, Kang SB. A case of diabetes mellitus treated with oriental and western medical combination therapy. Korean J Orient Int Med. 2004 ; 25(3) : 602-8.
11. Jung HS, Song BY, Lee CH, Yook TH. Effects of *Cinnamomum Cassia* and *Aconitum Carmichaeli's* pharmacopuncture and oral administration on blood sugar in type 2 diabetic mice. The Journal of Korean Acupuncture and Moxi-

- bustion Society. 2010 ; 27(5) : 1-12.
12. Pai HC, Tzeng CY, Lee YC, Chang CH, Lin JG, Cheng JT, Chang SL. Increase in plasma glucose lowering action of rosiglitazone by electroacupuncture at bilateral Zusanli acupoints (ST₃₆) in rats. *J Acupunct Meridian Stud.* 2009 ; 2(2) : 147-51.
 13. Chang SL, Lin KJ, Lin RT, Hung PH, Lin JG, Cheng JT. Enhanced insulin sensitivity using electroacupuncture on bilateral Zusanli acupoints (ST₃₆) in rats. *Life Sci.* 2006 ; 79(10) : 967-71.
 14. Chung CU, Lee YH, Kang SK. Preventive effect on development of diabetes and renoprotective Effect of *Acanthopanax Senticosus* Aqua-acupuncture in multiple low-dose streptozotocin-induced diabetic rats. *The Journal of Korean Acupuncture and Moxibustion Society.* 2003 ; 20(3) : 1-14.
 15. Ahn CB, Jang KJ, Yoon HM, Kim CH, Min YK, Song CH, Lee JC. Sa-ahm five element acupuncture. *J Acupunct Meridian Stud.* 2010 ; 3(3) : 203-13.
 16. 朱丹溪. 丹溪心法(下卷). 서울 : 大星文化社. 1982 : 503-9.
 17. Hashimoto J, Chonan K, Aoki Y, Nishimura T, Ohkubo T, Hozawa A et al. Pulse wave velocity and the second derivative of the finger photoplethysmogram in treated hypertensive patients: Their relationship and associating factors. *J Hypertens.* 2002 ; 20 : 2415-22.
 18. John Allen. Photoplethysmography and its application in clinical physiological measurement, *Physiol. Meas.* 2007 ; 28 : 1-39.
 19. Iketani Y, Iketane T, Tanakawa K, Murata M, Second derivate of photoplethysmogram in children and young people. *Jpn Circ J.* 2000 ; 64 : 110-6.
 20. Takazawa K, Fujita M, Yabe K, Saiki T, Kobayashi T, Maeda K et al. Clinical usefulness of the second derivative of a plethysmogram (acceleration plethysmogram). *J Cardiol.* 1993 ; 23 : 207-17.
 21. Kim SW, Lee JH, Nam KC, Kim SC, Cha EJ, Kim DW. Comparison of peripheral vascular compliance between normal and diabetic groups using the second derivative of photoplethysmogram. *The institute of electronics engineers of Korea.* 2007 ; 44(4) : 15-9.
 22. Oh HL, Cho JM, Jin ES, Kang HS, Choue CW, Kim KS, Song JS, and Bae JH. Clinical usefulness of the second derivative of a photoplethysmogram waveform(SDPTG). *Korean Circulation J.* 2003 ; 33(3) : 233-41
 23. Jose FR, Ricardo EG, Jorge AC, Ruben RR. Vascular responses to manual PC₆ acupuncture in nonsmokers and smokers assessed by the second derivative of the finger photoplethysmogram waveform. *Journal of acupuncture and meridian studies.* 2008 ; 1(1) : 58-62.
 24. Imanaga I, Hara H, Koyanagi S, Tanaka K. Correlation between wave components of the second derivative of plethysmogram and arterial distensibility. *Jpn Heart J.* 1998 ; 39 : 775-84.
 25. Dey L, Attele AS, Yuan CS. Alternative therapies for type 2 diabetes. *Alternative medicine review.* 2002 ; 7(1) : 45-58.
 26. King H, Aubert RE, Herman WH. Global burden of diabetes, 1995-2025: Prevalence, numerical estimates, and projections. *Diabetes Care.* 1998 ; 21 : 1414-31.
 27. Kim KJ, Lee BW, Kim HM, Shin JY, Kang ES, Cha BS, Lee EJ, Lim SK, Lee HC. Associations between cardio-ankle vascular index and microvascular complications in type 2 diabetes mellitus patients. *J Atherosclero Thromb.* 2010 ; 18 : 1-9.
 28. Izuhara M, Shiofi K, Kadota S, Baba O, Takeuchi Y, Uegaito T, Mutsuo S and Matsuda M. Relationship of cardio-ankle vascular index (CAVI) to carotid and coronary arteriosclerosis. *Circ J.* 2008 ; 72 : 1762-7.
 29. Manson JE, Coditz GA, Stampfer MJ, Willett WC, Krolewski AS, Rosner B, Arky RA, Speizer FE, Hennekens CH. A prospective study of maturity-onset diabetes mellitus and risk of coronary heart disease and stroke in women. *Arch Intern Med.* 1991 ; 151 : 1141-7.
 30. Gu K, Cowie CC, Harris MI. Diabetes and decline in heart disease mortality in US adults. *JAMA.* 1991 ; 281 : 1291-7.