ORIGINAL RESEARCH Do Far-infrared Saunas Have Cardiovascular Benefits in People with Type 2 Diabetes?

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ABSTRACT

OBJECTIVE: Far-infrared saunas are beneficial for the treatment of congestive heart failure, hypertension and obesity. As such, they may have a beneficial effect on cardiovascular (CV) health in those with type 2 diabetes. Our objective is to examine whether or not there are quantitative CV benefits from infrared sauna use.

METHODS: The intervention consisted of 20-minute, thriceweekly infrared sauna sessions, over a period of 3 months. The following CV risk factors were measured: weight, height, waist circumference, blood pressure (BPtru), glycated hemoglobin (A1C), fasting blood glucose and cholesterol profile. Baseline study parameters were measured within one week prior to commencing sauna sessions. Post-intervention measurements were collected between 1 and 3 days after the last sauna session.

RESULTS: Systolic blood pressure decreased by 6.4 mm Hg (124 ± 12 vs. 118 ± 15 mm Hg, 95% CI 0.01–12.71 p=0.05), and there was a trend toward decreased waist circumference (115.0 ± 13.4 vs. 112.7 ± 11.9 cm, 95% CI 0.4–5.1 p=0.10). All other measurements did not change significantly. There were no adverse events. Study completion rate was 75%.

CONCLUSION: Our results suggest that infrared sauna use may be beneficial for lowering blood pressure and waist circumference. Subject adherence to infrared sauna use is greater than adherence to other lifestyle interventions. The combination of favourable compliance/adherence, as

Address for correspondence:

Richard Beever, Faculty of Medicine, Department of Family Practice Box 98, Fraser Lake, British Columbia, Canada V0J 1S0 Tel: (250) 699-6225, Fax: (250) 699-6510 well as effectiveness in improving blood pressure and possibly waist circumference, makes infrared sauna therapy an attractive lifestyle option.

KEYWORDS: cholesterol, diabetes, hypertension, infrared sauna, waist circumference

RÉSUMÉ

OBJECTIF: Les saunas à infrarouge lointain sont utiles pour le traitement de l'insuffisance cardiaque congestive, de l'hypertension et de l'obésité. Il se pourrait donc qu'ils aient un effet salutaire sur la santé cardiovasculaire des personnes atteintes de diabète de type 2. Notre objectif était de déterminer si l'utilisation d'un sauna à infrarouge avait des bienfaits quantitatifs sur la santé cardiovasculaire.

MÉTHODES: L'intervention consistait en l'utilisation d'un sauna à infrarouge pendant 20 minutes trois fois par semaine pendant une période de trois mois. On a mesuré objectivement les facteurs de risque cardiovasculaire suivants : poids, taille, tour de taille, tension artérielle (tensiomètre BPtru), hémoglobine glycosylée (HbA_{1c}), glycémie à jeun et bilan du cholestérol. Les valeurs de départ ont été obtenues dans la semaine précédant la première utilisation du sauna et les valeurs finales, d'un à trois jours après la dernière utilisation du sauna.

RÉSULTATS : La tension artérielle systolique a baissé de 6,4 mm Hg (124 \pm 12 par rapport à 118 \pm 15 mm Hg; p = 0,05, IC de 95 % : 0,01 à 12,71) et il y a eu une tendance à la réduction du tour de taille (115,0 \pm 13,4 par rapport à

112,7 \pm 11,9 cm; p = 0,10, IC de 95 % : 0,4 à 5,1). Les autres paramètres n'ont pas changé de façon significative. Il n'y a pas eu d'effets indésirables. Soixante-quinze pour cent des sujets ont terminé l'étude.

CONCLUSIONS : Les résultats obtenus donnent à penser que l'utilisation d'un sauna à infrarouge pourrait contribuer à la réduction de la tension artérielle et du tour de taille. Les sujets sont plus fidèles à l'utilisation d'un sauna à infrarouge qu'à d'autres interventions axées sur le mode de vie. Ensemble, la fidélité à l'utilisation d'un sauna à infrarouge et l'efficacité de celui-ci pour la réduction de la tension artérielle et, possiblement, du tour de taille font de l'utilisation d'un sauna à infrarouge une option thérapeutique attrayante.

MOTS CLÉS : diabète, hypertension, tour de taille, cholestérol, sauna à infrarouge

INTRODUCTION

"The health consequences of obesity, diabetes and cardiovascular disease will overwhelm and cripple our healthcare system unless the current trend is stopped," state Emili and colleagues (1). Because the risk of coronary heart disease increases with multiple risk factors, means of reducing multiple risk factors may have a synergistic effect in the prevention and/or treatment of cardiovascular disease (CVD) (2).

Manufacturers of far-infrared saunas (FIRS) claim numerous health benefits, including weight loss, improving CV health, normalizing blood pressure (BP), lowering cholesterol, and reducing pain, stress and fatigue (3). If FIRS can indeed improve multiple risk factors, then their benefit in reducing CVD could be significant. FIRS are advertised in publications targeting Canadian physicians, and the evidence to support such claims is starting to accumulate (4-13); we have recently published a concise summary (14). FIRS are widely available to the public and cost between \$1000 and \$5000, depending on size and quality. They are also becoming increasingly available at gyms, spas and hotels.

Diabetes is a major risk factor for CVD (15,16). However, there is no published research examining the effects of FIRS exclusively in people with diabetes. Do FIRS have a beneficial effect on CV health in those with type 2 diabetes? We address this question and overcome the pitfalls of previous studies by employing a larger sample size and longer study duration, and by using validated measurement tools in a community-based study. This study is of importance to those who currently have diabetes or CVD. The implications will be of significant interest to healthcare providers, patients, manufacturers, regulatory agencies and consumers.

METHODS

Design

This was a sequential, longitudinal, interrupted time series study.

Intervention

We studied a Canadian Standards Association-approved Sunlight Armana 3 infrared sauna, in accordance with the manufacturer's instructions (Sunlight Saunas World Headquarters, Overland Park, Kansas, USA). Subjects were asked to attend 20-minute sauna sessions, 3 times per week, over a 3-month period during the winter of 2007/2008.

To determine if FIRS have beneficial effects on CV health, we measured height, weight, waist circumference (WC), hip circumference, BP, glycated hemoglobin (A1C), fasting blood glucose (FBG) and fasting lipid profile. BP was measured using the BPtru: 5 measurements taken 2 minutes apart. This has been shown to have accuracy similar to a 24-h ambulatory BP (17-19).

Baseline measurements were taken within one week prior to starting sauna sessions, and post-intervention measurements were taken between 1 and 3 days after the last sauna session, allowing adequate time for rehydration.

Subjects were asked to refrain from starting any new "diets" or herbal medications and to maintain their current exercise routine. An exercise routine and medication review was conducted during the baseline and follow-up interviews.

People with type 2 diabetes from the Fraser Lake Community Health Centre were invited to participate in this study. See Table 1 for exclusion criteria.

The Statistical Department at the University of British Columbia conducted the statistical analysis. A paired t-test was used to determine significance; p<0.05 was considered statistically significant. Due to the smaller sample size, our statistician advised to include finding with a p<0.10 as possibly significant. Based on previous studies regarding the effects of FIRS on BP, it was estimated that a sample size of 20 would be required to sufficiently power this study (6,8-12).

Both the University of British Columbia and the Northern Health Authority Ethics Review Boards approved this study.

RESULTS

Participant attenuation

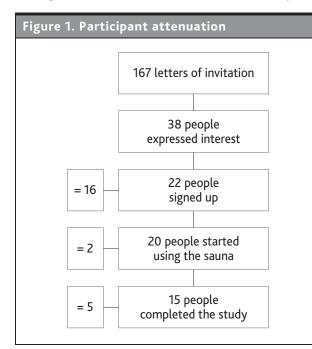
Letters of invitation were sent out to our population of patients with diabetes (167 people) (see Figure 1); 38 subjects expressed interest in participating. Twenty-two subjects signed up and completed the baseline measurements. Two were excluded, leaving 20 to participate in the study. The study subjects were all white; 14 were female and 6 were male; the average age was 66.5 years (range: 50–75

Table 1. Exclusion criteria					
 Absolute contraindications Anhydrosis. Inability to fit into sauna: although the sauna was a 3-person sauna, the door was relatively small (63.5 cm, 25"), so some of our more obese patients would not have been able to enter. Likewise, it was not wheelchair accessible. Communicable skin disease. Pregnancy. Although far-infrared treatment does not appear to be harmful to the pregnancy (20-22), weight gain and BP changes experienced during pregnancy would invalidate the results of the study. Unstable angina, recent myocardial infarction (30 days) and severe aortic stenosis. Medications via a patch delivery system (such as nicotine, fentanyl, nitroglycerine or contraceptive patches); the increased 					
 Any illness causing a fever. Newly discovered or currently If patients had BP >160/90 n family physician and removed 	ed an increased rate of delivery from the patch, leading to unwanted side effects. y uncontrolled diabetes, hypertension or hypercholesterolemia necessitating medical treatment. m Hg, A1C >9.0% or TC/HDL-C ratio >7.0 at baseline screening, they were referred to their d from the study, as initiation of pharmacological treatment could have invalidated findings. (These intinuing to use the sauna for the duration of the study if they chose, without further follow-up.)				
	ir sweating (such as beta-blockers and anticholinergics). I impair sweating (such as Parkinson's disease, multiple sclerosis, CNS tumours or autonomic				
A1C=glycated hemoglobin BP=blood pressure	CNS=central nervous system TC/HDL-C=total cholesterol high-density lipoprotein cholesterol ratio				

years). All 20 subjects began the study and 15 (75%) completed it. Of the 5 subjects who did not complete the study, 1 was lost to follow-up, 2 cited time-commitment factors and the other 2 were a couple who cited transportation and mobility problems.

Quality assurance

Baseline screening revealed 2 people with BP >160/90 mm Hg, A1C >9.0% or a TC/HDL-C ratio >7.0. They were



referred to their family physician and removed from the formal study, as initiation of pharmacological treatment would have invalidated the findings. There were no reported changes regarding exercise routines, diet, over-the-counter (OTC)/herbal supplements or medication prescriptions during the 3-month study period. Accordingly, improvements cannot be attributed to changes in exercise, food, OTC/ herbal supplements or medications.

The results are summarized in Table 2. Systolic BP decreased by 6.4 mm Hg (124 ± 12 vs. 118 ± 15 mm Hg, 95% CI 0.01–12.71 p=0.05). There was a trend toward a decreased WC of 2.3 cm (115.0 ± 13.4 vs. 112.7 ± 11.9 cm, 95% CI 0.4–5.1 p=0.10). There was also a trend toward a worsened TC/HDL-C ratio of 0.2 (4.2 ± 0.9 vs. 4.4 ± 0.9 , 95% CI 0.004–0.411 p=0.054). Weight, FBG, and triglyceride levels did not change significantly.

Adverse events

There were no adverse events. Specifically, there were no reported symptoms suggestive of pre-syncope, heat rash, heat exhaustion or heat stroke.

DISCUSSION

This study represents an improvement from previously published studies, in that it has a larger sample size (4,7,8,13), a substantially longer duration (4-6,8-13) and focused exclusively on people with type 2 diabetes. Unlike previously published studies examining the effect of FIRS on BP, our post-intervention measurements were taken at least

Table 2. Findings						
Measurement	Pre-study mean (SD)	Post-study mean (SD)	Mean improvement	p-value	95% CI	
Systolic BP, mm Hg	124 (12)	118 (15)	6.4	0.05*	0.01–12.71	
Diastolic BP, mm Hg	74 (9)	71 (10)	2.6	0.32	-2.8-7.9	
Pulse, bpm	71 (13)	68 (8)	3.0	0.49	-6.3-12.3	
FBG, mmol/L	7.4 (1.9)	7.5 (1.7)	-0.2	0.63	-0.94-0.59	
A1C, %	6.7 (0.7)	6.7 (0.8)	0	0.92	-0.32-0.30	
TC/HDL-C ratio	4.18 (0.9)	4.38 (0.9)	-0.2	0.05*	-0.41-0	
Fasting TGs, mmol/L	2.05 (0.8)	2.02 (0.8)	0.04	0.82	-0.31-0.38	
WC, cm	115.0 (13.4)	112.7 (11.9)	2.3	0.10	0.4–5.1	
Weight, kg	98.7 (18.0)	99.5 (17.9)	-0.8	0.26	-2.3-0.7	
BMI, kg/m²	35.1 (7.2)	35.5 (7.5)	-0.3	0.27	-1.0-0.3	

*Statistically significant

A1C=glycated hemoglobin BMI=body mass index BP=blood pressure FBG=fasting blood glucose TGs=triglycerides WC=waist circumference

24h after the last session, allowing sufficient time for rehydration (8,11). Another important difference is that our study was community-based; while this was associated with a lower completion rate than studies with inpatient populations, it was also more illustrative of the real-world uptake of sauna use as a therapeutic lifestyle intervention. The FIRS adherence rate of 75% is significantly better than adherence to other lifestyle change (23), and effective lifestyle modifications that have high patient uptake are key to preventing and treating the current epidemic of lifestyle-induced chronic disease (24,25). FIRS may be a novel therapeutic intervention in this regard.

Previous studies have shown that BP reduction in subjects with congestive heart failure is likely a result of improved endothelial function and increased nitric oxide production (10,12). BP control is the single most important riskreduction strategy for patients with type 2 diabetes (26-28). We have shown that FIRS are beneficial for lowering BP in those with type 2 diabetes. The clinical relevance of lowering systolic BP by 6.4 mm Hg is significant and well documented (26-33). As such, regular use of FIRS may serve as a useful nonpharmacological adjunct in treating hypertension.

Up to 90% of people with type 2 diabetes are overweight (34). Obesity is a national and global epidemic and a leading cause of morbidity and mortality (35-38). Our findings suggest that FIRS may reduce WC. The clinical relevance of lowering WC imparts significant benefits to those with obesity, diabetes, hypertension, coronary artery disease, hyperlipidema, obstructive sleep apnea, arthritis, metabolic syndrome and polycystic ovarian syndrome (29-31,35,37-44).

The thermoregulatory demands of maintaining homeostasis during FIRS therapy imparts endocrine and CV stress. Although many of our subjects were sedentary, a subjective theme became apparent: FIRS use was similar to a moderate exercise regimen, except that it was "much more relaxing" and was "like exercise without exercising." As such, FIRS may be an effective lifestyle adjuvant, especially for those finding it difficult to participate in traditional exercise programs.

Our results suggest that FIRS treatment is not effective for lowering weight, A1C, FBG, cholesterol or triglyceride levels. This strengthens the conclusions of previous studies, which have also found no effect on cholesterol or triglyceride levels, and clarifies those studies that have had conflicting results regarding changes in weight and fasting blood glucose (8-12). It should be noted that all our subjects were on a statin-type medication and that this is the standard of care. However, as their cholesterol levels were already lowered pharmaceutically, our cholesterol-lowering findings cannot be extrapolated to those not on a statin.

Although this study offers improvements over previously published studies, it has 3 main limitations. First, it is limited by a small sample size and relatively short duration. It was powered to detect changes in BP, but is likely underpowered to detect changes in other CV risk factor measurements. Second, community-based studies rely on volunteer subjects and may pre-select for motivated subjects who are more likely to be adherent to the study protocol, resulting in greater adherence rates than may otherwise be seen. It should be noted, however, that unlike most interventional studies that examine efficacy, this study relied entirely upon subject self-motivation to attend the study sessions-it was a study of real-life adherence. Third, this study is not a randomized, blinded, placebo-controlled trial. In studies examining sauna therapy, it would not be possible to have a blinded placebo-control group, and randomization was not a possibility given our sample size. We therefore chose the sequential, longitudinal interrupted time series cohort design, as it has the unique advantage of allowing subjects to serve as their own controls, thereby ensuring perfectly matched groups and allowing all subjects to participate in the intervention. This design is well-suited to small and remote centres, where subject recruitment is a significant barrier to research. A potential disadvantage of the study design is the presence of confounding variables that may affect the study population. For example, weight and BP have a tendency to increase over the winter months (45,46). This would have a negative effect on our data, leaving the impression that FIRS therapy was less effective than it actually was. However, it would also strengthen the validity of our positive findings.

Future studies are warranted. Such studies should have a larger sample size, allowing for increased statistical power and a randomized control group. Further studies may include more frequent interventions and/or longer study durations. Such studies may want to focus on subjects with CV risk factors such as hypertension, dyslipidemia, diabetes or obesity.

CONCLUSION

Our results suggest that FIRS use lowers BP and WC in those with type 2 diabetes. We found that the uptake of FIRS use was greater than the uptake of standard lifestyle interventions. The combination of favourable adherence and effectiveness makes FIRS therapy an attractive lifestyle option. In this study, FIRS did not lower weight, FBG, cholesterol or triglycerides; however, our sample size was relatively small, and further study is warranted.

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AUTHOR DISCLOSURE

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REFERENCES

- Emili A, Abushomar H, Nair K. Treating metabolic syndrome: lifestyle change or medication? *Can Fam Physician*. 2007;53: 1203-1205.
- Hoeg JM. Evaluating coronary heart disease risk: tiles in the mosaic. JAMA. 1997;277:1387-1390.
- 3. Advertisement: Physician Heal Thyself Soleil Sauna. Just for Canadian Doctors. 2006;Winter:2.
- 4. Masuda A, Kihara T, Fukudome T, et al. The effects of repeated thermal therapy for two patients with chronic fatigue syndrome. *J Psychosom Res.* 2005;58:383-387.
- Masuda A, Koga Y, Hattanmura M, et al. The effects of repeated thermal therapy for patients with chronic pain. *Psychother Psychosom.* 2005;74:288-294.
- 6. Kihara T, Biro S, Ikeda Y, et al. Effects of repeated sauna treatment on ventricular arrhythmias in patients with chronic heart failure. *Circ J.* 2004;68:1146-1151.
- Sugahara Y, Ishii M, Muta H, et al. Efficacy and safety of thermal vasodilation therapy by sauna in infants with severe congestive heart failure secondary to ventricular septal defect. *Am J Cardiol.* 2003;92:109-113.
- 8. Miyamoto H, Kai H, Nakamura H, et al. Safety and efficacy of repeated sauna bathing in patients with chronic systolic heart failure: a preliminary report. *J Card Fail*. 2005;11:432-436.
- 9. Nguyen Y, Naseer N, Frishman WH. Sauna as a therapeutic option for cardiovascular disease. *Cardiol Rev.* 2004;12:321-324.
- Kihara T, Biro S, Imamura M, et al. Repeated sauna treatment improves vascular endothelial and cardiac function in patients with chronic heart failure. J Am Coll Cardiol. 2002;39:754-759.
- Masuda A, Miyata M, Kihara T, et al. Repeated sauna therapy reduces urinary 8-epi-prostaglandin F(2alpha). Jpn Heart J. 2004;45:297-303.
- 12. Imamura M, Biro S, Kihara T, et al. Repeated thermal therapy improves impaired vascular endothelial function in patients with coronary risk factors. *J Am Coll Cardiol*. 2001;38:1083-1088.
- Biro S, Masuda A, Kihara T, et al. Clinical implications of thermal therapy in lifestyle-related disease. *Exp Biol Med (Maywood)*. 2003;228:1245-1249.
- 14. Beever R. Far-infrared saunas for treatment of cardiovascular risk factors: summary of published evidence. *Can Fam Physician*. 2009;55:691-696.
- Gerstein HC, Meltzer S. Preventive medicine in people at high risk for chronic disease: the value of identifying and treating diabetes. *CMAJ*. 1999;160:1593-1595.
- Kaur J, Singh P, Sowers J. Diabetes and cardiovascular diseases. *Am J Ther.* 2002;9:510-515.
- Mattu GS, Heran BS, Wright JM. Overall accuracy of the BpTRU-an automated electronic blood pressure device. *Blood Press Monit.* 2004;9:47-52.
- Beckett L, Godwin M. The BpTRU automatic blood pressure monitor compared to 24 hour ambulatory blood pressure monitoring in the assessment of blood pressure in patients with

hypertension. BMC Cardiovasc Disord. 2005;5:18.

- Greiver M. Improving diabetes care in my practice. Can Fam Physician. 2007;53:1897.
- 20. Hannuksela ML, Ellahham S. Benefits and risks of sauna bathing. *Am J Med.* 2001;110:118-126.
- Judge CM, Chasan-Taber L, Gensburg L, et al. Physical exposures during pregnancy and congenital cardiovascular malformations. *Paediatr Perinat Epidemiol.* 2004;18:352-360.
- Kauppinen K. Facts and fables about sauna. Ann N Y Acad Sci. 1997;813:654-662.
- Jones H, Ruggiero L, Edwards L. Diabetes stages of change. Methodology and study design. *Can J Diabetes Care.* 2001;25: 97-107.
- Gaede P, Videl P, Larsen N, et al. Multifactorial intervention and cardiovascular disease in patients with type 2 diabetes. *N Engl J Med.* 2003;348:383-393.
- Harris SB, Petrella RJ, Lambert-Lanning A, et al. Lifestyle management for type 2 diabetes. Are family physicians ready and willing? *Can Fam Physician*. 2004;50:1235-1243.
- 26. Snow V, Weiss KB, Mottur-Pilson C; Clinical Efficacy Assessment Subcommittee of the American College of Physicians. The evidence base for tight blood pressure control in the management of type 2 diabetes mellitus. *Ann Intern Med.* 2003;138: 587-592.
- Vajan S, Hayward RA. Treatment of hypertension in type 2 diabetes mellitus: blood pressure goals, choice of agents, and setting priorities in diabetes care. *Ann Intern Med.* 2003;138:593-602.
- UK Prospective Diabetes Study Group. Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). *Lancet*. 1998;352:837-853.
- Padwal R, Campbell N, Touyz RM; Canadian Hypertension Education Program. Applying the 2005 Canadian Hypertension Education Program recommendations: 3. Lifestyle modifications to prevent and treat hypertension. *CMAJ*. 2005;173:749-751.
- Quan A, Kerlikowske K, Gueyffier F, et al. Efficacy of treating hypertension in women. J Gen Intern Med. 1999;14:718-729.
- Bhavnani S, Nicholls S, Shi H, et al. Clinical benefit of intensive blood pressure lowering in obese patients with coronary artery disease. A Camelot substudy. J Clin Hypertens. 2007;9 (suppl A):66.
- Lackland DT, Gilbert G, Carter R, et al. Long-term survival by hypertension status for white and black men and women. *J Clin Hypertens*. 2007;9(suppl A):137.
- Staessen JA, Wang JG, Thijs L. What can be expected from optimal blood pressure control? J Hypertens Suppl. 2003;21:S3-9.
- Sigal RJ, Kenny G. Physical activity: 2003 clinical practice guidelines highlights. *Canadian Diabetes*. 2005;18(Spring):2,3,7.
- Kopelman PG. Obesity as a medical problem. *Nature*. 2000;404: 635-643.
- World Health Organization. Obesity and Overweight. Global Strategy on Diet, Physical Activity and Health. Geneva: WHO; 2005.

- 37. Lau DC, Douketis JD, Morrison KM, et al; Obesity Canada Clinical Practice Guidelines Expert Panel. 2006 Canadian clinical practice guidelines on the management and prevention of obesity in adults and children [summary]. CMAJ. 2007;176: S1-13.
- 38. Tjepkema M. Adult Obesity in Canada: Measured Height and Weight. Ottawa, ON: Statistics Canada; 2005.
- Kato J, Eto T, Kitamura K. Importance of body weight control and commitment by physicians in controlling blood pressure: a community-based observational study. *J Clin Hypertens*. 2007;9 (suppl A):134.
- 40. Foreyt JP. The role of lifestyle modification in dysmetabolic syndrome management. *Nestle Nutrition Workshop Series Clinical and Performance Program.* 2006;11:197-206.
- Douketis JD, Feightner JW, Attia J, et al. Periodic health examination, 1999 update: 1. Detection, prevention and treatment of obesity. Canadian Task Force on Preventive Health Care. CMAJ. 1999;160:513-525.
- Marshall K. Mosby's Family Practice Sourcebook Evidence Based Emphasis. Toronto, ON: Mosby, Inc.;2001:326-329.
- 43. Canadian Diabetes Association. Diabetes facts: the prevalence and costs of diabetes. Available at: http://www.diabetes.ca/ about-diabetes/what/prevalence/. Accessed May 15, 2010.
- Knowler WC, Barrett-Connor E, Fowler SE, et al; Diabetes Prevention Program Research Group. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. *N Engl J Med.* 2002;346:393-403.
- Argani H, Javanshir MR. Seasonal variations of blood pressure in hemodialysis and renal transplant recipients. *Transplant Proc.* 2004;36:148-149.
- 46. Woodhouse PR, Khaw KT, Plummer M. Seasonal variation of blood pressure and its relationship to ambient temperature in an elderly population. *J Hypertens*. 1993;11:1267-1274.