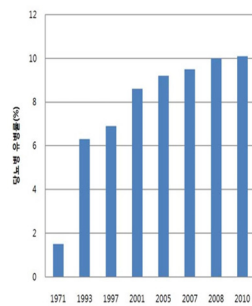
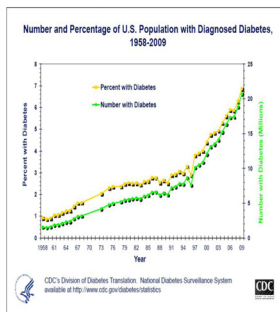


Improving Vascular Endothelial Function in Type 2 Diabetes: What is Optimal Exercise Intensity?

황 문 현
인천대학교

[세미나] 지역사회 체육 세미나

Prevalence: Type 2 Diabetes



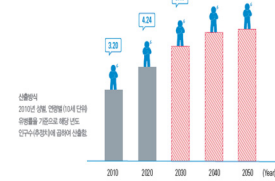
Prevalence: Type 2 Diabetes

FUTURE DIABETES POPULATION

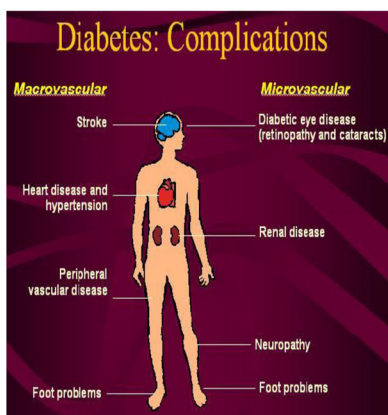
190%↑

2050년 당뇨병 추정 인구

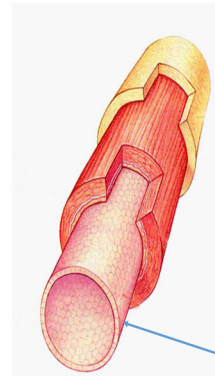
> 2005년 현재: 12% 병행자수
약 400만명으로 추정
> 2010년 7억 1000만~1억 4000만명으로
증가 400만명 약 2배 증가 예상



Diabetes & CV Complications

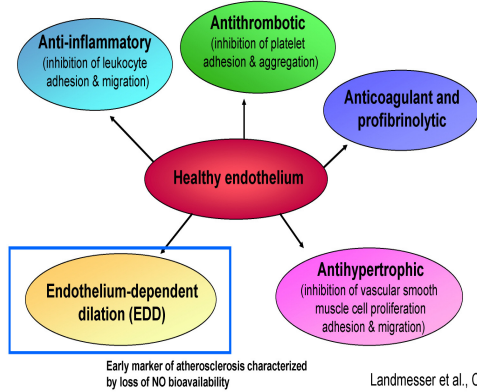


The vascular endothelium: triggering site for atherosclerosis

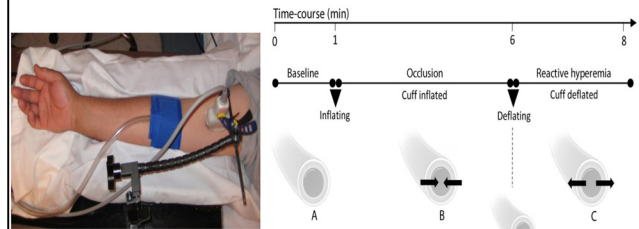


the vascular endothelium
(nitric oxide production)

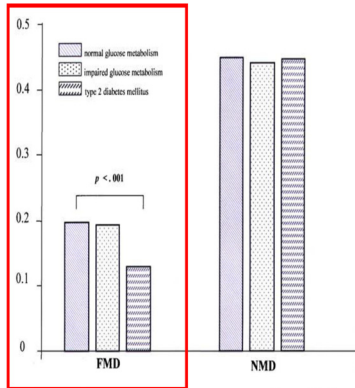
Healthy vascular endothelium inhibits atherogenesis



Endothelium-dependent dilation is assessed using flow-mediated dilation (FMD)

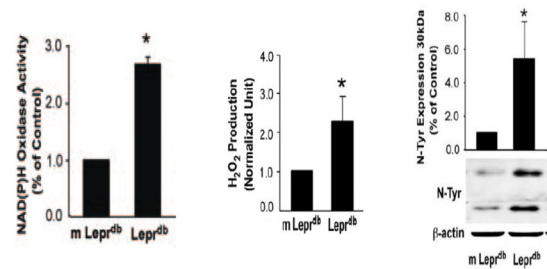


Endothelial Dysfunction in Type 2 Diabetes



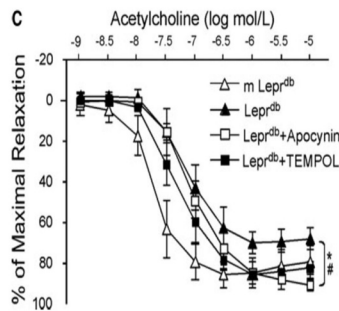
Henry et al., Atherosclerosis, 2004

Increased Oxidative Stress in Diabetic Vasculatures



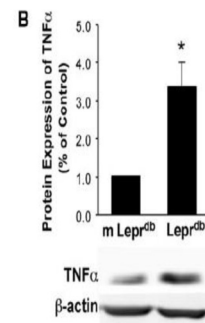
Zhang et al., ATVB 2009

Oxidative Stress-Mediated Endothelial Dysfunction in Diabetic Vasculatures



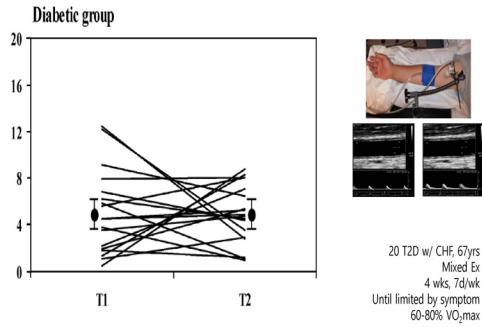
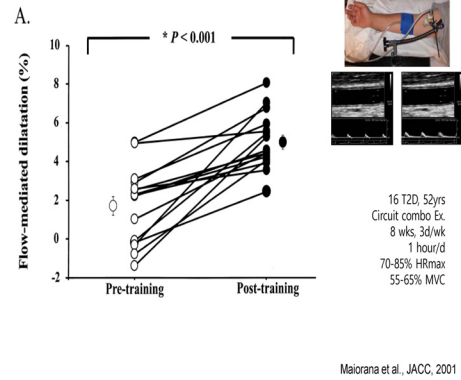
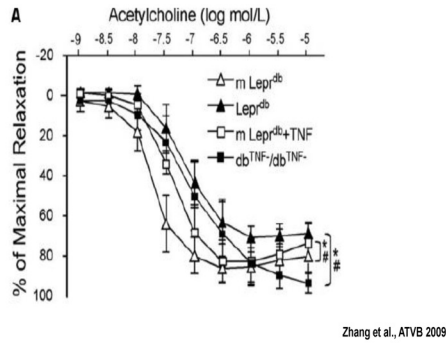
Zhang et al., ATVB 2009

Increased Inflammatory Cytokines in Diabetic Vasculatures



Zhang et al., ATVB 2009

Inflammation-Mediated Endothelial Dysfunction in Diabetic Vascatures



Effective exercise strategy for improving vascular endothelial function in type 2 diabetic patients?

AMERICAN COLLEGE
of SPORTS MEDICINE
AMERICAN DIABETES
ASSOCIATION

JOINT POSITION STATEMENT

SPECIAL COMMUNICATIONS

Exercise and Type 2 Diabetes

SUMMARY

Although physical activity (PA) is a key element in the prevention and management of type 2 diabetes mellitus (T2DM), many with this chronic disease do not become or remain regularly active. High-quality studies establishing the importance of exercise and fitness in diabetes were lacking until recently, but it is now well established that participation in regular PA improves blood glucose control and can prevent or delay T2DM, along with positively affecting lipid, blood pressure, cardiovascular events, mortality, and quality of life. Structured interventions combining PA and modest weight loss have been shown to lower T2DM risk by up to 50% in high-risk populations. Most benefits of PA on diabetes management are realized through acute and chronic improvements in insulin action, accomplished with both aerobic and resistance training. The benefits of physical training are discussed, along with recommendations for varying activities. PA-associated glucose management, diabetes prevention, gestational diabetes, and safe and effective practices for PA with diabetes-related complications.

diabetes, and amputation (261). Although regular physical activity (PA) may prevent or delay diabetes and its complications (10,46,89,112,176,208,259,294), most people with T2DM are not active (193).

In this article, the broader term "physical activity" (defined as "bodily movement produced by the contraction of skeletal muscle that substantially increases energy expenditure") is used interchangeably with "exercise," which is defined as "a subset of PA done with the intention of developing physical fitness (i.e., cardiovascular, strength, and flexibility training)." The intent is to recognize that many types of physical movement may have a positive effect on physical fitness, morbidity, and mortality in individuals with T2DM.

Diagnosis, classification, and etiology of diabetes.
Position Statement: American Diabetes Association (ADA) 2006

ACSM & ADA Position Stand: Exercise Recommendation for Type 2 Diabetes (Aerobic Exercise)

[2000년 Position Stand]

Mode: 당뇨병 중 하나인 말초신경이상 및 퇴행성관절염을 방지하기 위하여 **비충격적 활동 권장**

- 고정식자전거, 수영, 아쿠아로빅 등
- 합병증의 위험이 적다면 가벼운 걷기

Intensity: **low-to-moderate PA**(최대산소섭취량의 40-70% 수준)

Duration: 10-15min/session 부터 **30min/session**까지 점진적으로 증가
체중감소를 목적으로 한다면 최대산소섭취량의 50%에서 60분간 실시를 목표

Frequency: 3-5d/wk

[2010년 Position Stand]

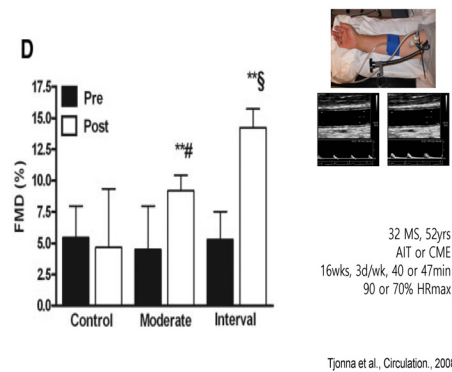
Mode: 가벼운 걷기와 같은 대근육 운동을 포함한 어떤 형태의 유산소성 활동도 가능
- **다양한 형태의 유산소 활동을 권장**

Intensity: **최소한 중강도**(최대산소섭취량의 50% 수준) 이상
- **고강도일수록 혈당 및 심혈관 건강상 이점**

Duration: **최소 주당 150분** 이상 권장
- 한번에 최소 10분간 지속할 수 있는 활동
- AHA와 US Federal Guideline 역시 중강도 일 경우 최소 주당 150분 이상 권장, 고강도 일 경우 최소 주당 60-75분 이상 권장

Frequency: 3-5d/wk, **혹은 매일**

Effect of HIIT vs. MICT on brachial artery FMD in MetS patients (pre-diabetes)



Effect of HIIT vs. MICT on brachial artery FMD in type 2 diabetic patients

Table 4. Vascular reactivity data

	SED (n=15)		CON (n=14)		INT (n=14)	
	Pre	Post	Pre	Post	Pre	Post
Flow-mediated dilatation						
Baseline brachial diameter (mm)	4.4 ± 0.6	4.5 ± 0.7	4.4 ± 0.7	4.4 ± 0.7	4.3 ± 0.6	4.5 ± 0.6
Peak brachial diameter (mm)	4.6 ± 0.4	4.7 ± 0.2	4.6 ± 0.4	4.7 ± 0.2	4.6 ± 0.4	4.9 ± 0.3*
Flow-mediated dilatation (%)	5.1 ± 1.3	5.6 ± 1.8	4.8 ± 1.6	6.1 ± 1.8*	5.4 ± 1.1	7.4 ± 0.9*†
Time to peak diameter (s)	59 ± 8	61 ± 14	64 ± 15	61 ± 12	61 ± 17	62 ± 14
Shear rate at rest (s ⁻¹)	36.2 ± 3.2	37.7 ± 3.0	34.8 ± 3.4	34.1 ± 2.8	37.7 ± 2.3	36.0 ± 2.6
Vascular resistance (AU)	0.61 ± 0.01	0.62 ± 0.01	0.61 ± 0.02	0.59 ± 0.02	0.62 ± 0.02	0.61 ± 0.01
Vascular conductance (AU)	1.65 ± 0.12	1.63 ± 0.14	1.64 ± 0.14	1.64 ± 0.15	1.62 ± 0.11	1.65 ± 0.17
Cutaneous blood flow						
Resting cutaneous blood flow (AU)	18.8 ± 2.8	20.1 ± 2.4	19.2 ± 2.3	18.1 ± 1.7	19.7 ± 1.9	18.4 ± 2.5
Maximal cutaneous blood flow (AU)	87.8 ± 14.7	89.6 ± 16.4	85.1 ± 12.8	91.5 ± 17.4	86.1 ± 18.8	89.9 ± 19.5†
Ratio of maximal cutaneous blood flow to resting cutaneous blood flow	4.4 ± 0.6	4.6 ± 0.9	4.2 ± 0.6	4.7 ± 0.6*	4.5 ± 0.5	5.1 ± 0.6*†

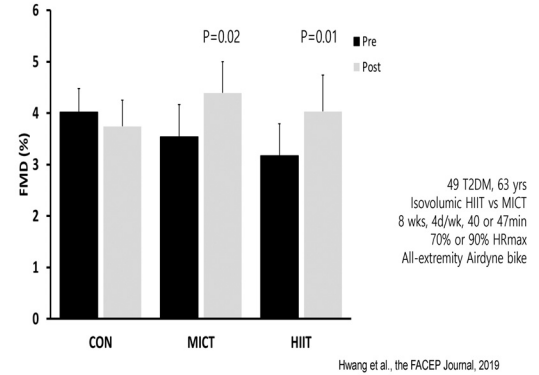
Data are means ± standard error of the mean.

*P < 0.05 vs Pre; †P < 0.05 vs SED; #P < 0.05 vs CON.

SED, sedentary control; CON, continuous aerobic exercise training; INT, interval aerobic exercise training; AU, arbitrary unit.

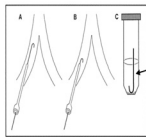
Mitrano et al., Scand J Med Sci Sports, 2014

Effect of HIIT vs. MICT on brachial artery FMD in type 2 diabetic patients



Vascular endothelial cell protein expression

1. Collect endothelial cells



2. Wash endothelial cells



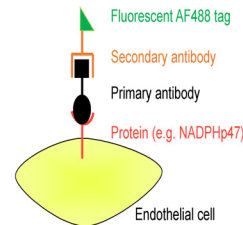
3. Fix and plate cells on slides



4. Dry and store slides for future immunofluorescence staining

Procedure described in detail in Colombo et al., J Appl Physiol, 2002

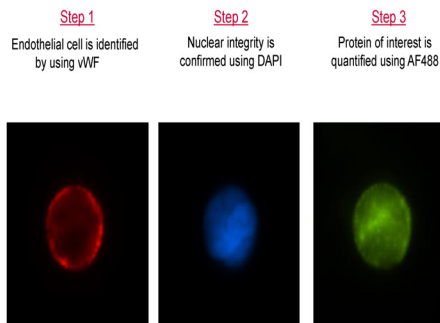
Vascular endothelial cell protein expression



- Rehydrate cells
- Block non-specific binding sites
- Stain with primary antibody for protein of interest (e.g., NADPH47)
- Stain with AF488 secondary antibody
- Stain with antibody for von Willebrand factor
- Stain with AF555 secondary antibody
- Stain nucleus using DAPI

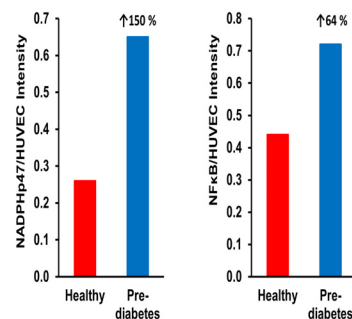
Procedure described in detail in Colombo et al., J Appl Physiol, 2002

Analysis of stained vascular endothelial cells



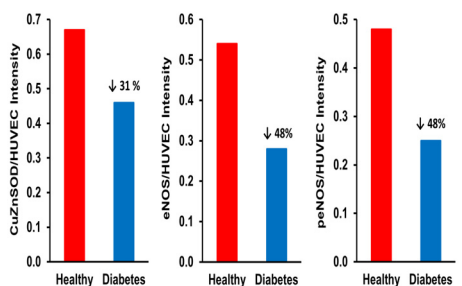
Procedure described in detail in Colombo et al., J Appl Physiol, 2002

Elevated ECPE of pro-atherogenic factors in prediabetic patients



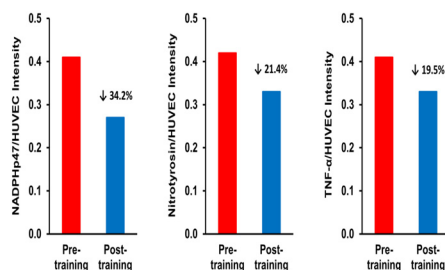
Hwang et al., preliminary data

Decreased ECPE of anti-atherogenic factors in type 2 diabetic patients



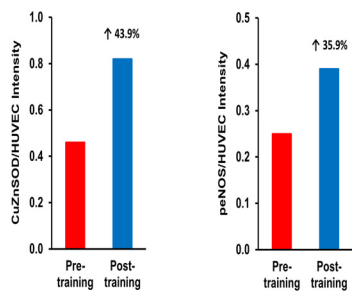
Hwang et al., preliminary data

HIIT decreased ECPE of pro-atherogenic factors in type 2 diabetic patients



Hwang et al., preliminary data

HIIT increased ECPE of anti-atherogenic factors in type 2 diabetic patients



Hwang et al., preliminary data