Obesity and Hypertension

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I have the following potential conflicts of interest to report:

- Stockholder of a healthcare company: NO
- Employment in industry: NO
- Owner of a healthcare company: NO
- Research Grants: NO
- Consulting and Speaker: Pfizer, Mylan, Terapie, Boehringer Ingelheim, Berlin Chemie, Menarini, Novartis, Sanofi, Zentiva, Bayer, Servier, Vifor Pharma, Alpha - Wasserman
- Others (please specify): NONE
Major Conflict of Interest
David
By Michelangelo

The World's Most Beautiful Man
David, after 3 years in USA
The Obesogenic Environment

Slide courtesy of Jason Halford, PhD, C. Psychol. (Health) AFBPsS.
Mona Lisa
Fernando Botero Angulo
Cause of Obesity

Simple equation...when you eat more than you use, it is stored in your body as “fat”.

Causes

- Global shift in how we eat and Physical inactivity
- Western diet of processed food
- Higher sugar, fat and calories in what we eat
- Less nutrients
- Reduced intake of vitamins and minerals
Wall-E

Captain B McCrea
Physical Inactivity
Wall-e Commanding Officers
"WE'VE JUST UPDATED THE FOUR BASIC FOOD GROUPS..."
What does obesity do to our bodies?

- With more people gaining too much weight...there are health issues to consider
  - Cardiovascular disease
  - Diabetes type 2
  - Musculoskeletal disorders
  - Cancers - endometrial, cervical and colon
  - Infertility
  - Gallstones
  - Premature death and disability
The current view of adipose tissue: secretory/endocrine organ with effects on different levels through the cardiovascular organ.

↑ IL-6
↓ Adiponectin
↑ Leptin
↑ TNFα
↑ Adipsin (Complement D)
↓ Adiponectin
↑ Lipoprotein lipase
↑ Agiotensinogen
↑ Insulin
↑ FFA
↑ Resistin
↑ Leptin
↑ Lactate
↑ Plasminogen activator inhibitor-1 (PAI-1)

Inflammation
Hypertension
Atherogenic dyslipidaemia
Type 2 diabetes
Atherosclerosis
Thrombosis

Lyon 2003; Trayhurn et al 2004; Eckel et al 2005
Obesity

- Obesity is associated with an increased risk of CV mortality
- Most prior studies examining CV risk have used BMI as the measure of obesity
  - BMI poorly characterizes central obesity
  - Waist circumference (WC) and waist-to-hip ratio (WHR) more strongly correlate with CV event rates

Figure 3: Association of BMI and waist-to-hip ratio with myocardial infarction risk
Vertical bars=95% CIs.
Prevalence and Age of Obesity

U.S. Prevalence of Obesity, by Age, 2009–2010

NOTE: Obesity in children defined as BMI at or above the age- and sex-specific 95th percentiles of 2000 CDC growth charts; obesity in adults defined as BMI at or above 30.

Physical Inactivity

![Graph showing prevalence of physical inactivity among adults by disease status.](image)

**Prevalence of Physical Inactivity Among Adults by Disease Status**

<table>
<thead>
<tr>
<th>Condition</th>
<th>Physical Inactivity (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neither condition</td>
<td>9.4</td>
</tr>
<tr>
<td>Obesity only</td>
<td>13.5</td>
</tr>
<tr>
<td>Arthritis only</td>
<td>16.1</td>
</tr>
<tr>
<td>Both Arthritis and Obesity</td>
<td>22.7</td>
</tr>
</tbody>
</table>

Data Source: 2007 and 2009 Behavioral Risk Factor Surveillance Survey, combined 50 states and the District of Columbia
Obesity is a Major Risk Factor for Hypertension

Glucose Metabolism
IGT / T2D
Insulin Resistance
Syndrome X
Dyslipidaemia
CVD

Obesity

Hypertension

Glucose Metabolism
IGT / T2D

Insulin Resistance
Syndrome X

Dyslipidaemia

CVD
Hypertension

- Excess body weight is associated with an increase in blood pressure
- The prevalence of hypertension is substantially higher in obese compared to lean populations
- Modest weight gain is also associated with increasing blood pressure
Changes in Systolic & Diastolic BP with Age

Prevalence of hypertension (>140/90) by BMI - NHANES III, 1988-1994

% of population

<25: 16, 18
25-26: 22, 23
27-29: 24, 25
>30: 31, 38

Women | Men

BMI (kg/m²)

NTFPTO, Arch Intern Med 2000; 160: 898-904
Overall prevalence of hypertension in the Southern Community Cohort Study (SCCS)

![Graph showing prevalence of hypertension associated with various factors including BMI, smoking, alcohol consumption, family history of heart disease, depression, diabetes, and high cholesterol.](image)

The processes leading to hypertension in the obese are incompletely understood:

- Increased sympathetic nervous system activity
- Activation of the renin-angiotensin system
- Insulin resistance

Have all been proposed as possible mechanisms.

*Sharma et al. J. Hypertension 2002;20:1873-1878*
Hemodynamic and Renal Changes in Obesity-Induced Hypertension

- Studies in experimental animals
  - A highly reproducible rise in BP is observed with excess weight gain induced by a high-fat diet in dogs and rabbits.
  - The metabolic, endocrine, cardiovascular, and renal changes caused by dietary-induced obesity in these experimental animals closely mimic the changes observed in obese humans
  - Some of these changes occur rapidly during overfeeding
  - Become obscured by pathological changes.

Hall JE. The kidney, hypertension, and obesity. Hypertension. 2003;41:625–633. doi: 10.1161/01.HYP.0000052314.95497.78
Hemodynamic and Renal Changes in Obesity-Induced Hypertension

- glomerular hyperfiltration early in obesity may be replaced by a gradual
  - because renal injury
  - nephron loss occur in association with
  - prolonged hypertension,
  - diabetes mellitus and dyslipidemia

- disruption of central nervous system (CNS) signaling pathways that link obesity with sympathetic nervous system (SNS) activation and hypertension.

- rodent models of obesity, such as those with melanocortin 4 receptor (MC4R) or leptin gene mutations, have normal or reduced SNS activity and decreased BP, despite inflammation, insulin resistance, dyslipidemia, and other metabolic changes associated with obesity


### Hemodynamic, Neurohormonal, and Renal Changes in Obese Humans, Compared With Lean Subjects, and in Experimental Animal Models of Obesity Caused by a High-Fat Diet

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Humans</th>
<th>Dogs</th>
<th>Rabbits</th>
<th>Rats</th>
<th>Mice</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arterial pressure</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
</tr>
<tr>
<td>Heart rate</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
</tr>
<tr>
<td>Baroreflex sensitivity</td>
<td>↓</td>
<td>↓</td>
<td>↓</td>
<td>↓</td>
<td>↓</td>
</tr>
<tr>
<td>Cardiac output</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
</tr>
<tr>
<td>( \text{VO}_2 ) mL/min</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
</tr>
<tr>
<td>( \text{VO}_2 ) mL/min kg(^{-1}) body weight</td>
<td>↓</td>
<td>↓</td>
<td>↓</td>
<td>↓</td>
<td>↓</td>
</tr>
</tbody>
</table>

**Cardiac hypertrophy**

<table>
<thead>
<tr>
<th>Type</th>
<th>Humans</th>
<th>Dogs</th>
<th>Rabbits</th>
<th>Rats</th>
<th>Mice</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eccentric</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
</tr>
<tr>
<td>Concentric</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
</tr>
<tr>
<td>Cardiac diastolic function</td>
<td>↓</td>
<td>↓</td>
<td>↓</td>
<td>↓</td>
<td>↓</td>
</tr>
<tr>
<td>Muscle blood flow (resting)</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
</tr>
<tr>
<td>Muscle blood flow reserve</td>
<td>↓</td>
<td>↓</td>
<td>?</td>
<td>?</td>
<td>?</td>
</tr>
<tr>
<td>GFR(^{*})</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
</tr>
<tr>
<td>Renal blood flow(^{*})</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
</tr>
<tr>
<td>Renal Na(^{+}) reabsorption</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
</tr>
<tr>
<td>Sympathetic activity†</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
</tr>
<tr>
<td>Renal</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
</tr>
<tr>
<td>Cardiac</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
</tr>
</tbody>
</table>

**Visceral obesity**

- Leptin/POMC
- RAAS and MR activation

**Renal compression**

- Renal Na\(^{+}\) reabsorption
- Macula Densa Feedback

**Blood pressure**

- Impaired renal-pressure natriuresis
- Blood pressure

**Chronic Kidney Disease**

**Metabolic disorders**

- Insulin resistance
- Glucose intolerance
- Dyslipidemia
- Inflammation
- Lipotoxicity
Neuroimmune system in hypertension and obesity

- SFO-subfornical organ of the brain responsible for secreting a series of neurotransmitters and hormones including angiotensin and vasopressin.

- PVN-paraventricular nuclei responsible with increase sympathetic response.
Neuroimmune system in hypertension and obesity

- The enhanced inflammation within mediobasal hypothalamus is then thought to contribute to alterations in metabolism (Zhang et al., 2008)
- glucose homeostasis (Posey et al., 2009; Milanski et al., 2012)
- more recently, to cardiovascular regulation (Purkayastha et al., 2011)

- Consistent with this, Purkayastha et al. determined that hypothalamic Iκκ-β and NFkB represents a key mechanism linking the consumption of high-fat diet to the dysregulation of energy, glucose and cardiovascular homeostasis.
- Further, inflammation specifically within propiomelanocortin neurons, which are particularly important for the regulation of energy balance, may contribute to blood pressure regulation,
Fat is bad

I wish I lived in a world where mosquitoes would suck FAT instead of blood.
Hypertension
Left ventricular Hypertrophy

Obesity is also a major determinant of left ventricular (LV) hypertrophy and congestive heart failure, independent of blood pressure

Sharma et al. J. Hypertension 2002;20:1873-1878
Increased prevalence of left ventricular hypertrophy (LVH)

Subjects (%)

- Normal weight
- Overweight (BMI >27 kg/m²)

*p<0.0001*

*p<0.05*

Probability of LVH by number of associated metabolic risk factors: the HyperGEN

Metabolic risk factors:
- Obesity
- Diabetes
- Dyslipidemia

Normotensive vs. Hypertensive
Fat infiltration can influence magnitude of LV mass and geometry
Potential determinants of concentric LV geometry

Severe obstructive sleep apnea elicits concentric left ventricular geometry
Giovanni Cioffi, Tiziano Edoardo Russo, Carlo Stefanello, Alessandro Selmi, Francesco Furlanello, Dana Cramariuc, Eva Gerdts and Giovanni de Simone

Elevated C-Reactive Protein in Patients With Obstructive Sleep Apnea
Abu S.M. Shamsuzzaman, MBBS, PhD; Mikolaj Winnicki, MD, PhD; Paola Lanfranchi, MD; Robert Wolk, MD, PhD; Tomas Kara, MD; Valentina Accurso, MD; Virend K. Somers, MD, PhD

Masked Hypertension
A Phenomenon of Measurement
Stanley S. Franklin, Eoin O’Brien, Lutgarde Thijs, Kei Asayama, Jan A. Staessen

<table>
<thead>
<tr>
<th>Normal Weight (n = 111)</th>
<th>Overweight (n = 113)</th>
<th>Obese (n = 223)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Constrictor geometry (%)</td>
<td>6.9</td>
<td>10.4</td>
</tr>
<tr>
<td>LV hypertrophy (%)</td>
<td>3.5</td>
<td>12.4</td>
</tr>
<tr>
<td>Inappropriate LV mass (%)</td>
<td>6.3</td>
<td>9.8</td>
</tr>
</tbody>
</table>
The 2 types of hearts

Hypertension, Obesity, OSA

Fig. 3. Relationships between obesity, OSA, disease mechanisms, and disease conditions. Solid lines show recognized associations, and dashed lines show possible associations.

(Gami 2003)
Obesity influences possibility to control BP.

### Table 4  Independent correlates of uncontrolled blood pressure in the whole population sample at the time of last available visit

<table>
<thead>
<tr>
<th></th>
<th>P value</th>
<th>OR</th>
<th>Lower</th>
<th>Upper</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (year)</td>
<td>&lt;0.002</td>
<td>1.01</td>
<td>1.00</td>
<td>1.02</td>
</tr>
<tr>
<td>Female sex</td>
<td>&lt;0.02</td>
<td>1.18</td>
<td>1.02</td>
<td>1.36</td>
</tr>
<tr>
<td>Initial SBP (×5 mmHg)</td>
<td>&lt;0.0001</td>
<td>1.10</td>
<td>1.09</td>
<td>1.12</td>
</tr>
<tr>
<td>Heart rate (beats/min)</td>
<td>&lt;0.0001</td>
<td>1.02</td>
<td>1.01</td>
<td>1.03</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>&lt;0.0001</td>
<td>1.04</td>
<td>1.03</td>
<td>1.06</td>
</tr>
<tr>
<td>Plasma creatinine (×5 μmol/l)</td>
<td>&lt;0.001</td>
<td>1.03</td>
<td>1.01</td>
<td>1.04</td>
</tr>
<tr>
<td>Triglycerides (mmol/l)</td>
<td>&lt;0.0001</td>
<td>1.17</td>
<td>1.08</td>
<td>1.27</td>
</tr>
<tr>
<td>Number of drugs</td>
<td>&lt;0.0001</td>
<td>1.27</td>
<td>1.16</td>
<td>1.39</td>
</tr>
<tr>
<td>Diuretics (%)</td>
<td>&lt;0.0001</td>
<td>0.73</td>
<td>0.62</td>
<td>0.86</td>
</tr>
<tr>
<td>RAS-blockers (%)</td>
<td>&lt;0.002</td>
<td>0.77</td>
<td>0.66</td>
<td>0.91</td>
</tr>
<tr>
<td>Statins (%)</td>
<td>&lt;0.003</td>
<td>0.79</td>
<td>0.68</td>
<td>0.92</td>
</tr>
</tbody>
</table>

Multivariate analysis including data detected at the time of the last available visit (with the exception of baseline SBP); diabetes, fasting glucose, high-density lipoprotein cholesterol, smoking status, β-blockers, Ca²⁺-channel blockers, α-blockers did not enter the model (all P > 0.1). BP, blood pressure; CI, confidence interval; Exp(B), exponentiation of the B coefficient; OR, odds ratio; RAS-blockers, renin–angiotensin system blockers.

5 years follow-up; 4612 hpt patients without prevalent CV disease; 43% women; 53 ±11 years.

De Marco M, de Simone G et al. J Hypertens 2011;30:188–193
Is Obesity always Bad?
The Impact of Obesity on the Short-Term and Long-Term Outcomes After Percutaneous Coronary Intervention: The Obesity Paradox?

Luis Gruberg, MD, Neil J. Weissman, MD, FACC, Ron Waksman, MD, FACC, Shmuel Fuchs, MD,
The obesity-mortality paradox in elderly patients with angiographic coronary artery disease: a report from the ET-CHD registry

Acta Cardiol 2015; 70(4): 479-486  doi: 10.2143/AC.70.4.3096897

P: 0.015

BMI group
- < 21.0
- 21.0-23.9
- 24.0-26.9
- 27.0-29.9
- >= 30.0

CV death

Cumulative Incidence (%) vs Years

Relative hazard ratio vs Body mass index
Obesity Paradox In Pts With Hypertension an IHD

Obesity Paradox in ACS

Take home message

• Obesity and hypertension are conditions closely linked.

• There are several physiopathological links to hypertension in obese patients

• Obesity exaggerates LV response to increased hemodynamic load, throughout the effect of non-hemodynamic mechanisms elicited by visceral adiposity.

• Fat mass is as important as, and perhaps more important than, fat-free mass to promote increase in LV mass, which is especially evident in women, due to their body composition.

• Hypertension gets resistant in obese patients and associates with other comorbidities which interfere in the physiopathology as treatment options of hypertension

• Effectively controlling BP is difficult without decreasing body weight.
But before I finish, because I come from a Bear’s land …
Which one do you think will be healthier?
Time changes everything
The Bear has the most “healthy fat”
We need fat people ...

BE NICE TO FAT PEOPLE
ONE DAY THEY MIGHT SAVE YOUR LIFE
Thank You!