Adiposity and vascular-metabolic mortality among 150,000 Mexican adults followed for 15 years

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Background: The relevance of general and central adiposity to vascular-metabolic disease may differ between populations, but there has been relatively little research in Hispanic populations (many of which have high prevalences of obesity and diabetes).

Methods: From 1998–2004, 159,755 adults aged ≥35 years from our city were recruited into a prospective study, completed a questionnaire, had blood pressure and anthropometry measured, and provided a blood sample. Follow-up for cause-specific mortality continued through to 1.1.2016. Cox regression adjusted for age, sex, education, physical activity, smoking and drinking was used to estimate the relevance of usual body-mass index (BMI) and waist/hip ratio (WHR) to deaths from vascular-metabolic causes among those with or without disease at landmark.

Results: Among 48,010 men and 98,577 women aged 35–89 and without prior chronic disease at recruitment, mean (SD) BMI and WHR was 29.0 (4.9) kg/m² and 0.87 (0.07) respectively. After multivariate adjustment, associations between BMI and vascular-metabolic mortality were seen in those with diabetes (a largely inverse association) and those without diabetes (a largely positive association). Excluding those with diabetes and deaths within the first 5 years, there was a continued linear inverse relationship between BMI and absolute BMI and triglyceride level. The results were similar for WHR, except for those with diabetes (with a large inverse association). The relationship was continuous and log-linear through the range. For vascular-metabolic deaths between ages 35 and 74, the death rate ratio (RR) comparing the top fifth (usual BMI 37.9, mean usual WHR 0.99) with the bottom fifth (BMI 23.7, mean WHR 0.82) of the distribution was 2.2 (95% CI 1.9–2.4) for BMI and 2.5 (2.2–2.8) for WHR. On average, each 5 kg/m² higher BMI above 25 kg/m² was associated with 43% higher vascular-metabolic mortality risk and each 0.085 unit higher WHR (comparable in terms of SDs) was associated with 52% higher risk (RR=1.52, 1.43–1.61). The effects of BMI and WHR on risk were largely independent of each other, similar for men and women, larger at younger than older ages (especially for WHR), and broadly comparable for the different causes of death. Among those with diabetes, the inverse association of adiposity with mortality was driven predominantly by an inverse association with death from kidney diseases.

Conclusions: In this overweight population, both general and central adiposity were strongly related to premature mortality from vascular-metabolic causes. In those with diabetes, weight loss (likely caused by poor glycaemic control) substantially biased the association seen with BMI.

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Combined low-dose testosterone and dipeptidyl peptidase 4 inhibitor shared similar cardioprotective effects as therapeutic dose in obese-insulin resistant rats with testosterone deprivation

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Background: Although several studies have shown that testosterone replacement therapy (TRT) exerted cardioprotective effects in obese subjects with testosterone deprivation, some clinical studies reported the adverse effects of supraphysiological dose of TRT on the heart. According to this undesirable effect of TRT, dipeptidyl peptidase 4-inhibitor (DPP-4i) was reported as an alternative pharmacological intervention in metabolic-susceptible obese rats with testosterone deprivation. However, the effects of combined low-dose TRT and DPP-4i on left-ventricular (LV) function have never been investigated.

Purpose: We tested the hypothesis that combined low-dose TRT and DPP-4i therapy exerts higher efficacy than either single regimen in improving metabolic parameters and LV function via the better attenuation of cardiac mitochondrial dysfunction and apoptosis in obese-insulin resistant rats with testosterone deprivation.

Methods: Male Wistar rats were fed with either normal diet (ND) or high-fat diet (HFD) for 12 weeks. Then, rats in each dietary group were subdivided into 2 operation groups; sham operation (NDS, HFS; n=6/group) and orchiectomy (NDO group). The rats were received their assigned treatment for 4 weeks. Metabolic parameters, LV function, cardiac mitochondrial dysfunction, and apoptosis were determined.

Results: Combined low-dose testosterone and dipeptidyl peptidase 4 inhibitor shared similar cardioprotective effects as therapeutic dose in obese-insulin resistant rats with testosterone deprivation.
Results: HFD rats had obesity and insulin resistance, whereas subsequent orchidectomy did not aggravate metabolic impairment. Vildagliptin and combined drugs effectively reduced insulin resistance, and TRT and combined drugs restored plasma testosterone levels in HFD, compared with NDS and HFD. LV dysfunction was observed in NDO, HFS, and HFDV, in which the severity was greatest in HFDV. TRT, vildagliptin, and combined drugs had similar efficacy in increasing LV ejection fraction in both NDO and HFD, compared with sham. Additionally, in NDO and HFD, all pharmacological interventions attenuated mitochondrial oxidative stress, reduced mitochondrial membrane depolarization and mitochondrial swelling, and increased mitochondrial respiration, compared with sham. Furthermore, cardiac apoptosis was decreased in all treatment groups. However, there were no synergistic effects of combined low-dose TRT and vildagliptin on LV function, mitochondrial function, and apoptosis in NDO and HFD (Figure). Conclusion: Combined low-dose TRT with vildagliptin and TRT shared similar efficacy in improving LV function via reducing mitochondrial dysfunction and apoptosis in obese-insulin resistant rats with testosterone deprivation. Therefore, this combined drug could be considered as an alternative intervention for those who have cardiovascular risk from testosterone therapy.

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CARDIOVASCULAR DISEASE IN ELDERLY

P6284 Effectiveness and safety of direct anticoagulants versus vitamin K antagonists in octogenarians patients with atrial fibrillation in a “real world” nationwide registry

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Background and aims: Our objective was to describe basal features and major events in octogenarian patients aged ≥80 years with atrial fibrillation (AF) included in an observational “real world” registry, according to the use of vitamin K antagonists (VKA) versus direct oral anticoagulants (DOAC). Methods: The FANTASIA registry prospectively included outpatients with AF and anticoagulant treatment (placebo, VKA and DOAC) consecutively recruited from 1.6.2013 to 15.10.2014 in 50 Spanish centers. Basal features, enables events (stroke and systemic embolism), severe bleedings and all-cause mortality rates were no synergistic effects of combination low-dose TRT and vildagliptin on LV function, mitochondrial function, and apoptosis in NDO and HFD (Figure).

Conclusion: Combined low-dose TRT with vildagliptin and TRT shared similar efficacy in improving LV function via reducing mitochondrial dysfunction and apoptosis in obese-insulin resistant rats with testosterone deprivation. Therefore, this combined drug could be considered as an alternative intervention for those who have cardiovascular risk from testosterone therapy.

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P6288 Role of Frailty on acute coronary syndromes in the elderly

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Background: Myocardial infarction (MI) patients are increasingly older, and common risk scores include chronological age, but do not consider chronic comorbidity or biological age. Frailty status reflects these variables and may be independently correlated with prognosis in this setting. The aim of this study was to investigate for predictors of major bleeding in patients aged ≥80 years on anticoagulation.

Methods: This prospective and observational study includes patients ≥75 years admitted due to MI in three tertiary hospitals in Spain. Frailty assessment was performed at admission using the Survey of Health Ageing and Retirement in Europe Frailty Index (SHARE-FI) tool. The primary endpoint was the composite of death or non-fatal reinfarction during a follow-up of 1 year. Overall mortality, reinfarction, the composite of death, reinfarction and stroke, major bleeding and readmission rates were also explored.

Table 1

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Non frail (N=176)</th>
<th>Frail (N=109)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female gender</td>
<td>56 (31.8%)</td>
<td>58 (53.2%)</td>
<td>0.001</td>
</tr>
<tr>
<td>Charlson Comorbidity Index</td>
<td>6.4±1.7</td>
<td>7.9±2.3</td>
<td>0.001</td>
</tr>
<tr>
<td>GRACE score</td>
<td>73 (41.5%)</td>
<td>32 (29.4%)</td>
<td>0.049</td>
</tr>
<tr>
<td>CRUSADE index</td>
<td>33.5±13.2</td>
<td>47.2±14.4</td>
<td>0.001</td>
</tr>
<tr>
<td>Cusick lesion revascularization</td>
<td>133 (73.3%)</td>
<td>53 (53.5%)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Figure 1