Bone and Mineral Metabolism
OSTEOPOROSIS AND VITAMIN D
Understanding Why Older People with Low Trauma
Fractures Die Prematurely
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OR13-03
There is increasing evidence that all proximal and not just
hip fractures are associated with increased mortality risk.
However, the cause of this increased mortality is unknown.
We sought to determine the post-fracture trajectories of
subsequent hospital admissions and mortality to develop
an understanding of why patients with non-hip fractures
die prematurely.
This nationwide Danish population-based study included
all individuals aged 50+ years who sustained an incident
frailty fracture between 2001 and 2014. High-trauma
fractures or individuals with fracture prior to 2001 were
excluded. Fracture patients were matched 1:4 by sex, age
and comorbidity status with non-fracture subjects alive at
the time of fracture. Comorbidities included 33 unique med-
cical conditions of the Charlson or Elixhauser comorbidity
index. We modelled the contribution of specific fractures on
the risk of subsequent admissions or death within the fol-
lowing 2 years.
There were 212,498 women and 95,372 men with frac-
ture followed by 30,677 and 19,519 deaths, respectively
over 163,482 and 384,995 person-years of follow up. Mean
age at fracture was 72± 11 for women and 75± 11 for men.
Proximal fractures including hip, femur, pelvis, rib, clavicle
and humerus had increased mortality compared with their
matched non-fracture counterparts with HRs ranging from
1.5-4.0, while distal fractures such as ankle, forearm, hand
or foot fractures had similar or lower mortality risk.
Almost 75% of men and 60% of women had ≥1 comorbidity.
For every additional comorbidity, risk of mortality increased
for all fracture types. However, only for proximal fractures
did the fracture itself independently increase mortality risk
over and above co-morbidity status.
The 2-yr post fracture admission and mortality patterns
differed between proximal and distal fractures. Proximal,
but not distal fracture subjects had greater risk of any
major hospital admission (including cardiovascular di-
sease, cancer, stroke, diabetes, pneumonia and pulmonary
disease) within 2 years compared with their non-fracture
counterparts. Distal fractures in general had similar admis-
sion patterns as their non-fractured matched counterparts.
Furthermore, 2 year mortality risk was increased for prox-
imal fractures whether or not they were admitted to hos-
pital post fracture. By contrast, mortality risk was similar
or reduced for distal fractures compared with non-fracture
controls.
This study has only confirmed the increased mor-
tality following proximal fractures but has demonstrated
differing clinical trajectories between proximal and distal
fractures that contribute to this increased mortality. These
findings provide important insights as to why proximal
fracture subjects die prematurely that may lead to specific
avenues for intervention.

Neuroendocrinology and Pituitary
NEUROENDOCRINE & PITUITARY PATHOLOGIES
Growth Hormone Deficiency and Replacement
Therapy: Association with Health-Related
Physical Fitness
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SUN-310
Objective: To compare health-related physical fitness (HRPF)
in patients with severe adult growth hormone defi-
ciency (AGHD) according to the deficiency onset phase, and
to evaluate the effects of a six-months human growth hor-
mone (rhGH) replacement therapy on HRPF, in a subgroup
of patients. Methods: First arm: cross-sectional observa-
tional study at baseline of naive rhGH multiple pituitary
hormonal deficiency (MPHD) hypopituitarism patients -
adult-onset growth hormone deficiency (AO-GHD) versus
child onset growth hormone deficiency (CO-GHD). Second

arm: a 6-month intervention clinical trial in a selected group of a non-randomized, non-controlled cohort. HRPF was evaluated by measuring isokinetic and isometric torque. A sub-group analysis was performed among mood disorder patients without a diagnosis of overt hypothyroidism, comparing euthyroid patients (TSH 0.3-4) and patients with sub-clinical hypothyroidism based on TSH 4-10.

Results: The cohort included 26,722 patients, mean age 46.3 years, 79.5% Caucasian, 68% females, and mean BMI 30. Mean PHQ-9 score was 8.2, 10% patients had severe depression (PHQ-9 >20), and 51% were on antidepressants and 26% on mood stabilizers. Mean TSH was 2.85, 19% patients had a diagnosis of hypothyroidism, and 20% patients were on THR. Patients with severe depression were more likely to have a higher mean TSH (p=0.06), be on antidepressants (p= <0.0001), and have a higher BMI (p=0.0003). There was a positive correlation between TSH and PHQ-9 score (p= 0.04). TSH was associated with severe depression, odds ratio 1.006 (1.003-1.009), after adjusting for potential co-variates. Hypothyroid patients who were on THR had a lower mean PHQ-9 score (p= <0.0001) as compared to hypothyroid patients not on THR. Patients with TSH from 7-10 had a higher PHQ-9 score as compared to those who had a TSH from 4-7 (p= <0.003).

Conclusion: Severe depression was associated with higher TSH. Subclinical hypothyroidism with TSH above 50th percentile was associated with higher PHQ-9 scores. Future RCTs should evaluate the effect of THR in (a) patients with severe depression and (b) patients with mood disorders who have subclinical hypothyroidism.

Diabetes Mellitus and Glucose Metabolism

IMPACTS OF METABOLISM ON CLINICAL CHALLENGES

Mild Physiologic Hyperglycemia Does Not Affect Glucose Mediated but Impairs Insulin-Mediated Suppression of Plasma Glucagon in Healthy Normal Glucose Tolerant Subjects

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OR26-07

Plasma glucagon levels are regulated by plasma glucose concentrations as well as intra-islet and circulating insulin concentrations. Hyperglycemia adversely affects skeletal muscle and hepatic insulin sensitivity (glucotoxicity). However, the effect of physiologic hyperglycemia on glucose-mediated and insulin-mediated suppression of glucagon is not known. The aim of the present study was to evaluate effect of chronic (48 or 72 hours) physiologic increase (+45 mg/dl) in plasma glucose concentration on the suppression of plasma glucagon concentration in healthy NGT individuals: 12 without family history of T2DM (FH-) (9M/3F, age = 50± 4 yrs, BMI = 27 ± 1 kg/m²) and 8 with FH of T2DM (FH+) (4M/4F, age = 48±2, BMI = 26±1 kg/m²).

Subjects received an OGTT and 2-step hyperglycemic (+125 and +300 mg/dl) clamp (duration of each step = 80 minutes) before and after 72 hour glucose infusion. On another occasion subjects participated in a 3-step hyperinsulinemic (10, 20, 40 mU/m² min) euglycemic clamp before and after a 48 hour glucose infusion. Plasma insulin and C-peptide concentrations were obtained every 2-5 minutes during each hyperglycemic clamp step and plasma glucagon concentrations were measured every 10 minutes. The ratio

Thyroid

HPT-AXIS AND THYROID HORMONE ACTION

The Association Between Thyroid Stimulating Hormone and Severe Depression: A Historical Cohort Study

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SAT-457

Introduction: Hypothyroidism is implicated in the pathophysiology and clinical course of mood disorders. This study aimed to investigate the association between TSH and severe depression. Methods: The historical cohort included all consecutive adult patients (≥ 18 years) who had a TSH and PHQ-9 questionnaire data within 6 months of index visit, between October 2016 and July 2019, at the University of Utah Health. Data on demographics, hypothyroidism, TSH, PHQ-9, thyroid hormone replacement (THR), and antidepressant medications were extracted electronically. T-test and chi-square were used to compare continuous and categorical variables respectively. Logistic regression and one-way ANOVA were used to evaluate the association between TSH and depression severity. A sub-group analysis was performed among mood disorder patients without a diagnosis of overt hypothyroidism, comparing euthyroid