Terapia di supporto in corso di terapia ormonale

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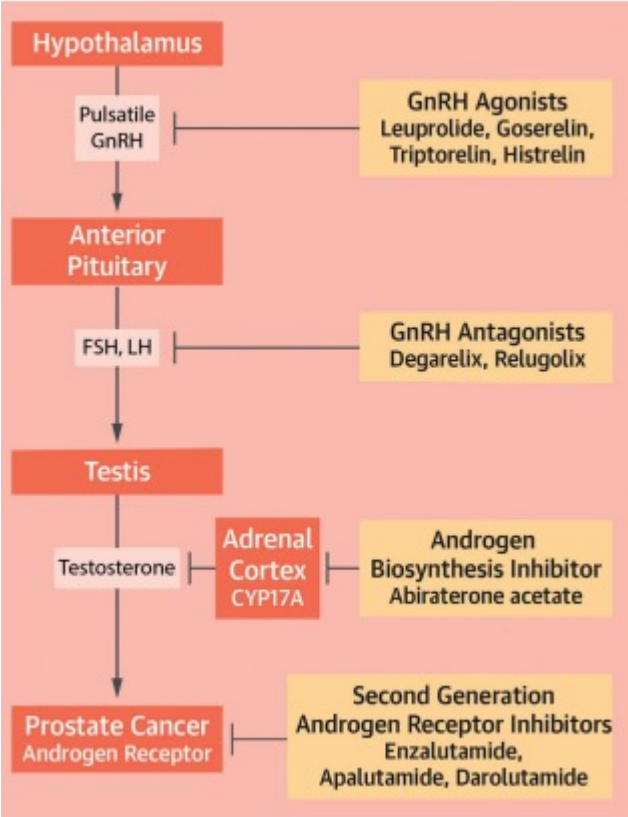
Aviano (PN)

Understanding of the adverse events (AEs) with ADT is critical!

- While ADT is integral to long-term disease control in PCa management, the drop in serum T levels is associated with AEs that can have QoL impacts



SIDE EFFECTS OF ADT

What physicians commonly tell	What patients see	What patients feel	What patients don't see
Loss of libido	Weight gain	Depression and emotional lability	Loss of bone density
Erectile dysfunction	Gynecomastia	Cognitive dysfunction	Metabolic syndrome
Hot flashes	Loss of muscle mass and strength	Fatigue, lack of energy, lack of initiative	Cardiovascular disease
	Shrinkage of penis and testicles		
	Hair changes		

Effects of ADT on Sexual Function

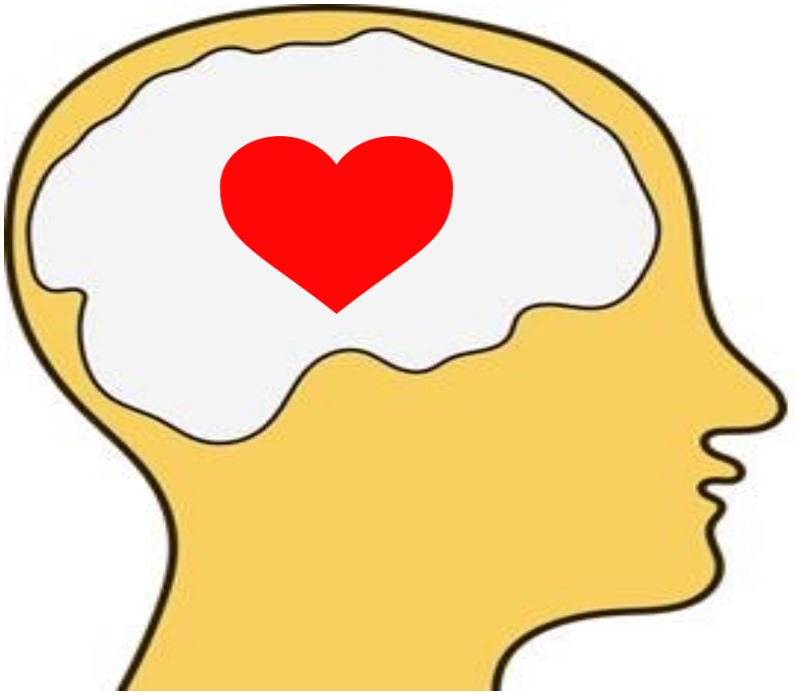
- Loss of libido and erectile dysfunction (ED) are major sexual health concerns associated with ADT
  - Degree of ED while on ADT is affected by pretreatment sexual function and libido changes
  - As sexual function is impacted by physiology and psycho-emotional issues, referral to psychology or counseling services with a focus on sexual health may be considered for the patient and their partners

LOSS OR LOWERING OF LIBIDO (SEX DRIVE)

- No magic pill to improve libido
- Lower libido is age related

How to enhance your libido?

- Exercise
- Enhance Intimacy
- Mindfulness
- Sensate Focus
- Simmering



ERECTILE DYSFUNCTION (ED)

Pharmacological, mechanical, or other interventions may be considered based on patient characteristics and preferences

Erectile Dysfunction Treatments:

- Oral medications (e.g. Sildenafil, Tadalafil)
- Vacuum pump erection devices
- Penile injections (e.g. Alprostadil)

Note! It is still possible to orgasm without an erection

ERECTION=ERECTION, ORGASM=ORGASM, ERECTION≠ORGASM

HOT FLASHES

Commonly occur after the first 2 months of starting ADT

Vasomotor symptoms, primarily hot flashes, are reported in up to 90% of men on ADT

What worsens hot flashes?

- Diet: avoid alcohol, spicy food, and caffeine (coffee, tea, colas, chocolate…etc.)
- Heat: stay cool and hydrated
- Stress: try to relieve stress

What can help with my hot flashes?

- Wear sweat wicking material
- Sleep with layers that can be removed and use a fan
- Massage and acupuncture
- Follow a regular exercise program
- Relaxation and Cognitive Behavioral Therapy (CBT)

HOT FLASHES

Other things people try:

- Soy foods
- Flaxseed
- Vitamin E
- Black Cohosh
- Garlic
- Ginseng

ADT-Associated Vasomotor Symptoms

Agents in use for treatment of hot flashes in men receiving ADT are associated with side effects

Medication	Common doses used for hot flashes	Common AEs
Megestrol acetate	20 mg PO qd	Weight gain, CV risk (DVT/PE), cost
Venlafaxine	75 mg PO qd	Feelings of being activated/jittery if not titrated properly Suicidal ideation Withdrawal issues
Paroxetine	…	Weight gain, loss of libido, suicidal ideation, withdrawal issues
Clonidine	…	…
Gabapentin	300 mg at bedtime or 100 mg every 8 hours	Drowsiness, dyspepsia
Medroxyprogesterone	150 mg IM	Increased risk of thrombotic issues

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GYNECOMASTIA

• Gynecomastia and breast tenderness have been reported by 12.7% to 28.6% of patients taking LHRHa

• Embarrassment associated with gynecomastia can result in increased social isolation and reduced engagement in physical exercise

Tamoxifen

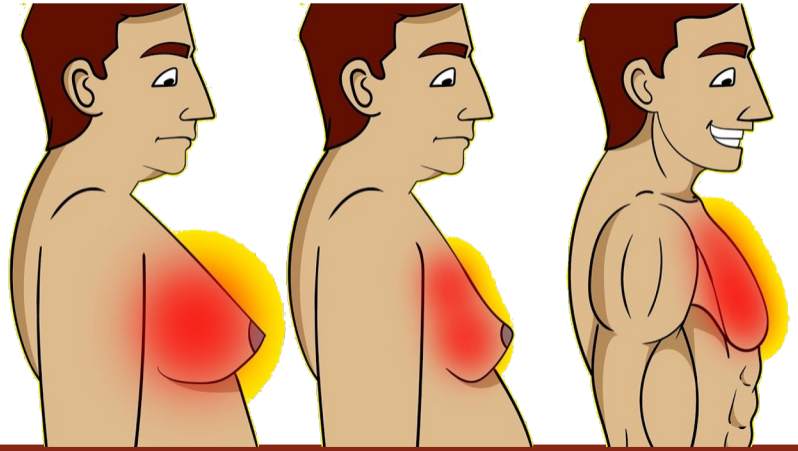
Prophylactic radiation therapy

GYNECOMASTIA

Treatment strategies to prevent and reduce gynecomastia and/or breast pain caused by antiandrogen therapy for prostate cancer

Statement from the DEGRO working group prostate cancer

Pirus Ghadjar[1] · Daniel M. Aebersold[2] · Clemens Albrecht[3] · Dirk Böhmer[1] · Michael Flentje[4] · Ute Ganswindt[5] · Stefan Höcht[6] · Tobias Hölscher[7] · Arndt-Christian Müller[8] · Peter Niehoff[9] · Michael Pinkawa[10] · Felix Sedlmayer[11] · Daniel Zips[8] · Thomas Wiegel[12] · Prostate Cancer Expert Panel of the German Society of Radiation Oncology (DEGRO) and The Working Party Radiation Oncology of the German Cancer Society (DKG-ARO)



- Prophylactic RT using 1 × 10 Gy or 2 × 6 Gy significantly reduced the rate of gynecomastia but not breast pain
- Daily dose of 20 mg TMX is the most effective prophylactic dose
- Prophylactic daily TMX is more effective than TMX given at the onset of gynecomastia
- Both prophylactic RT and TMX can reduce the risk of gynecomastia and/or breast pain with TMX being more effective (especially when symptoms are already present);
- Side effects after TMX including dizziness and hot flushes must be taken into account

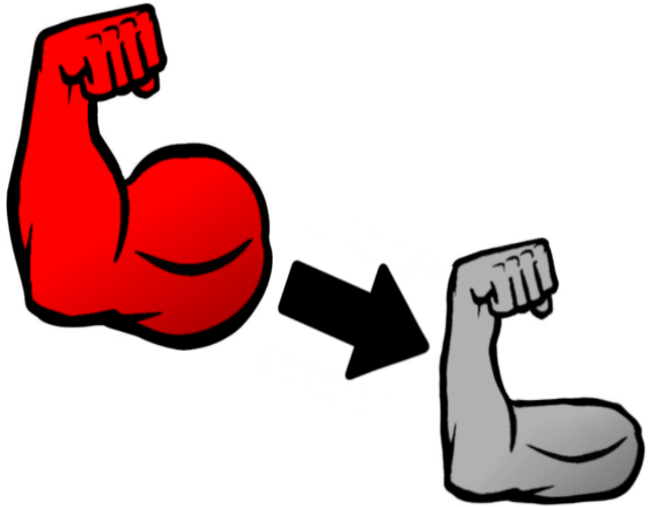
WEIGHT GAIN AND ASSOCIATED CHANGES

- More than 40% of men are overweight at diagnosis
- Common to gain up to 10 kg over 6-9 months due to increased appetite
- Increase in body fat especially at waist, hips, thighs
- Loss of muscle mass and strength
- Weight is difficult to lose even if ADT is stopped!
- Need to be physically active-aerobic and resistance exercise
- Engage in healthy lifestyle habits

LOSS OF MUSCLE MASS AND STRENGHT

Muscle-related AEs associated with ADT include:

- Lean body mass reduction (1%-4%; mainly from upper/lower limbs) and increase in fat mass (10%-20%) within first 12 months of ADT
- Decline in muscle strength and endurance (mainly upper limbs) within first 6 months of treatment
- Effects on muscle tissue is non-uniform across various muscle groups; for instance, ADT is associated with significantly greater increases in intramuscular fat within the gluteus maximus, but no significant change in gluteus medius and calf muscle volume at 12 months, compared to controls



ADT-associated musculoskeletal syndrome

- Muscle and joint aches and pains within 3 months of initiating ADT
- Could be associated with muscle wasting and tendons and ligaments thinning

Nonpharmacological

- Aerobic and resistance exercise
- Acupuncture x2 per week and then x6 weekly

Pharmacological

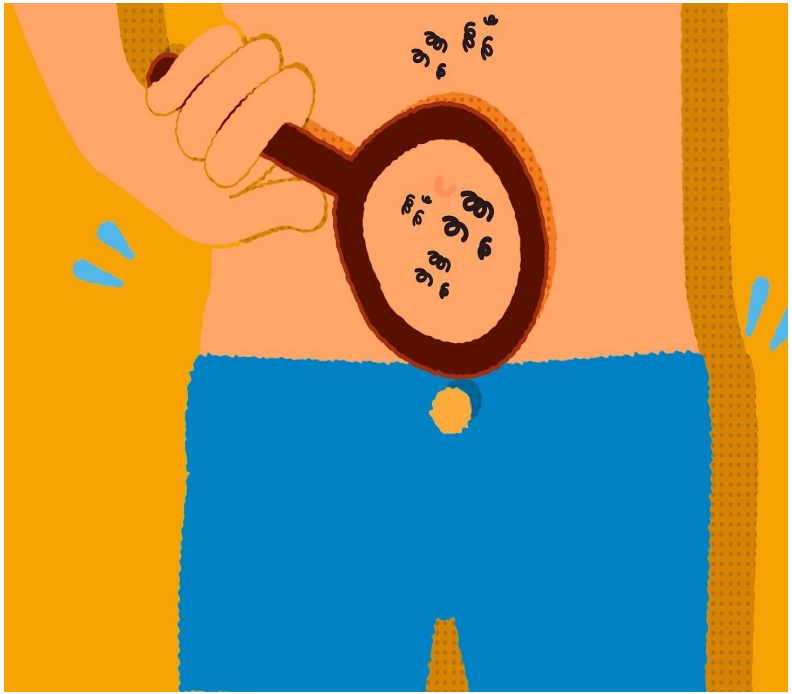
- NSAIDS 400 mg Ibuprofene x3 day for 5 days then 200-400 mg if needed
- Duloxetine (Cymbalta) 300 mg/day can increase to 60 mg/day if needed

SHRINKAGE OF PENIS AND TESTICLES

- Genital shrinkage: penis length, girth and testicular volume
- Apoptosis of trabecular smooth muscle
- Impaired veno-occlusive mechanism
- Fibrotic changes
- **Usually stops 12-18 months after starting ADT**

HAIR CHANGES

- Thinning or loss of body hair on trunk, arms, legs
- Beard softer
- May or may not be bothersome
- Not a health issue although it can be distressing if not informed
- **Reversible if ADT is stopped!**



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Neuropsychiatric Effects Associated with ADT

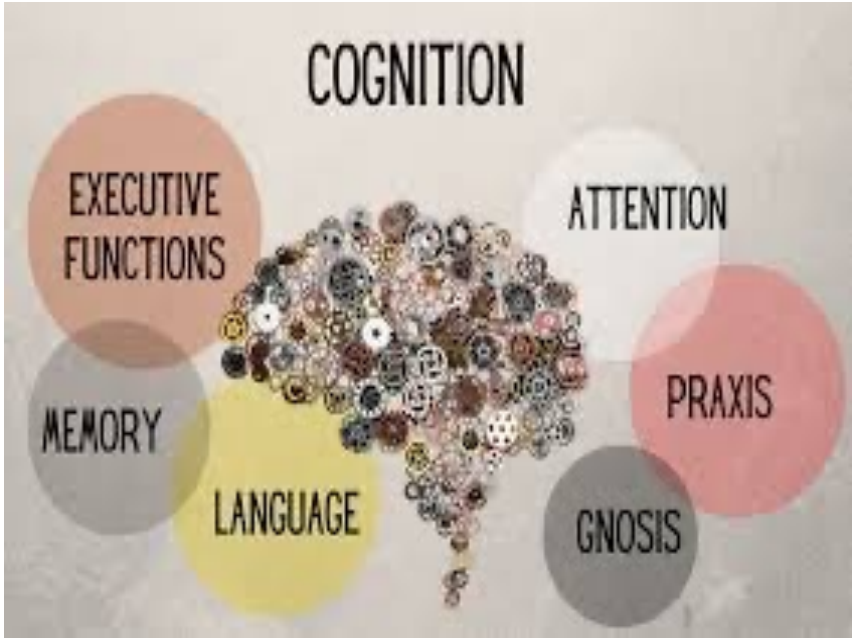
- Studies suggest an association between ADT and depression and/or cognitive dysfunction
  - However, depression is common in men with cancer
  - The impact of ADT on cognitive dysfunction is unclear
- In the NCCN guidelines, the potential link between ADT and depression and cognitive function are noted

DEPRESSION

- Acknowledge emotional lability is to be expected
- Major depression is seen in 13% of men on ADT and is 8 times higher than the general male population
- Prior history of depression is a risk factor
- Risk of depression increased with duration of ADT
- Anti-depressant if needed
- Exercise impacts mood in a positive way

COGNITIVE FUNCTION

- Impact on a small number of patients
- Typically affects spatial memory (e.g. where did I park the car?)
- Counselling services
- Exercise!
- Reduce clutter in living space
- Reduce alcohol and other depressants



FATIGUE

- Feeling of weariness, tiredness, or lack of energy that does NOT always improve with rest
- May affect your ability to do daily activities
- No medication is known to effectively reduce fatigue
- Exercising improves fatigue, social functioning, and mental health

FATIGUE

	Current Exercise and Nutrition Guidelines	Current Weight Loss Guidelines
 Aerobic training	150 min/week of moderate intensity exercise or 75 min/week of vigorous intensity exercise	300 min/week of moderate intensity exercise or 150 min/week of vigorous intensity exercise
 Resistance training	Minimum two strength training sessions/week	

RPE Scale	Rate of Perceived Exertion
10	**Max Effort Activity** Feels almost impossible to keep going. Completely out of breath, unable to talk. Cannot maintain for more than a very short time.
9	**Very Hard Activity** Very difficult to maintain exercise intensity. Can barely breath and speak only a few words
7-8	**Vigorous Activity** Borderline uncomfortable. Short of breath, can speak a sentence.
4-6	**Moderate Activity** Breathing heavily, can hold short conversation. Still somewhat comfortable, but becoming noticeably more challenging.
2-3	**Light Activity** Feels like you can maintain for hours. Easy to breathe and carry a conversation
1	**Very Light Activity** Hardly any exertion, but more than sleeping, watching TV, etc

nutrients 2021

Using Exercise and Nutrition to Alter Fat and Lean Mass in Men with Prostate Cancer Receiving Androgen Deprivation Therapy: A Narrative Review

SIDE EFFECTS OF ADT

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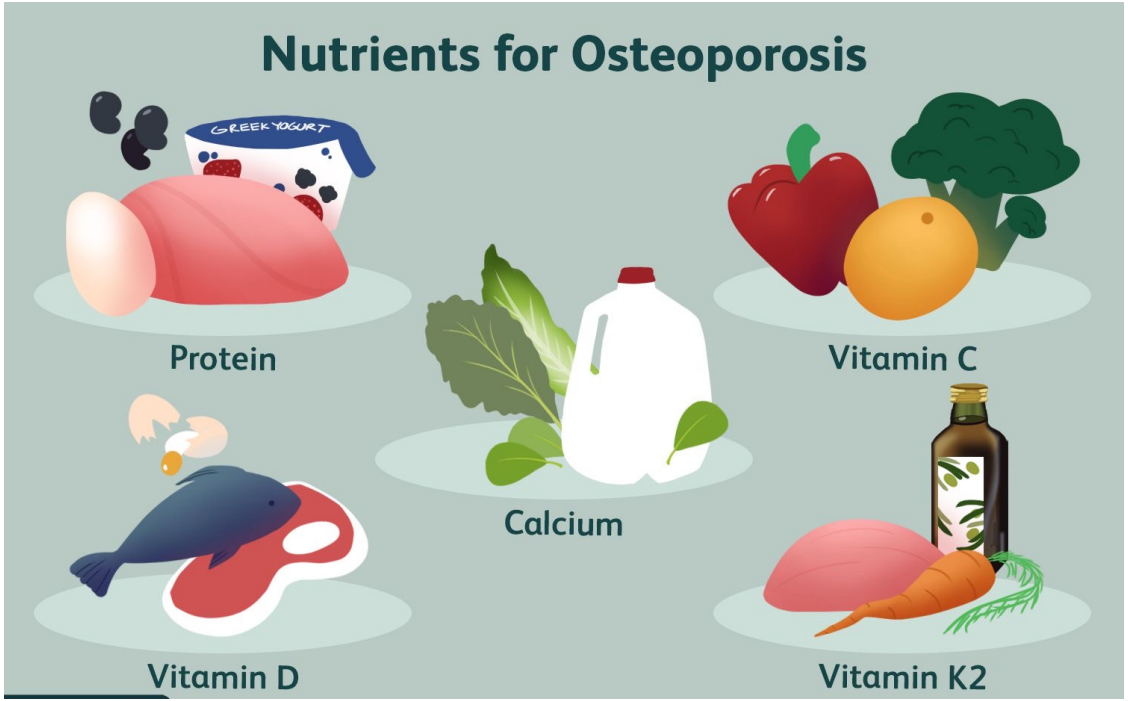
LOSS OF BONE DENSITY

- Skeletal AEs associated with ADT include:
  - **Decline in bone mass density (BMD),** with a maximum decrease of 5%-10% within the first year
  - **Annual bone loss of 2%-8% for the lumbar spine and 1.8%-6.5% for the femoral neck**
  - **Increased risk for osteoporotic fractures**; around 1 in 5 men receiving ADT experience an osteoporotic fracture within the first 5 years of treatment

LOSS OF BONE DENSITY

Bone health
Supervised resistance exercises
Lifestyle modifications (eg, smoking cessation, diet, decreasing alcohol intake)
Calcium and vitamin D supplementation
DEXA scan at baseline (within 6 months of initiating ADT) and at least once every 2 years for follow-up; evaluate fracture risk using the FRAX calculator
Bisphosphonates/RANK-L inhibitors when needed

Lifestyle modifications



LOSS OF BONE DENSITY

- All patients on ADT need to ensure they are receiving adequate amounts of Calcium and Vitamin D
    - **1200 mg Calcium** (not to exceed 2000 mg/day)
    - **1000 IU Vitamin D** (not to exceed 4000 IU/day)

  *unless serum vitamin D levels are low and being followed by a physician
- Men with moderate to high risk of fracture at 10-years should be offered drug therapy
    - **Denosumab 60mg SC every 6 months** (Must have good dental hygiene!)

LOSS OF BONE DENSITY

At the Initiation of ADT Evaluation for Any History of Trauma-Induced Fractures and Risk Factors for Osteoporosis [49]
BMD assessment with DXA scan and subsequent scoring with FRAX [49]
DXA scan or FRAX score only is not recommended. The following factors should be incorporated [49,53,54]
Age
BMD
History of corticosteroid therapy
Medical history of bone metastasis or fragility disease or treatment
Physical disability or risk factors of fall
Evaluations Recommended for Monitoring Skeletal Health (Perform at Baseline and Every 12–18 months Afterward) [54,59]
BMD measurement using DXA scan during the first 24 months of ADT
Bone turnover markers (e.g., serum ALP level)
Serum calcium levels
Serum vitamin D levels
Serum PTH levels
Height, weight, BMI
In the case of lumbar pain or loss of height, perform spine radiography and imaging studies

ADT: androgen-deprivation therapy; ALP: alkaline phosphatase; BMD: bone mineral density; BMI: body mass index; DXA: dual-energy X-ray absorptiometry; FRAX: fracture risk assessment tool; PTH: parathyroid hormone.

cancers

MDPI

Review

Pathophysiology of Bone Loss in Patients with Prostate Cancer Receiving Androgen-Deprivation Therapy and Lifestyle Modifications for the Management of Bone Health: A Comprehensive Review

Tae Jin Kim [1] and Kyo Chul Koo [2,*]

FRAX® Fracture Risk Assessment Tool

Home | Calculation Tool | Paper Charts | FAQ | Refe

Calculation Tool

Please answer the questions below to calculate the ten year probability of fracture with BMD.

Country: UK Name/ID: About the risk factors

Questionnaire:

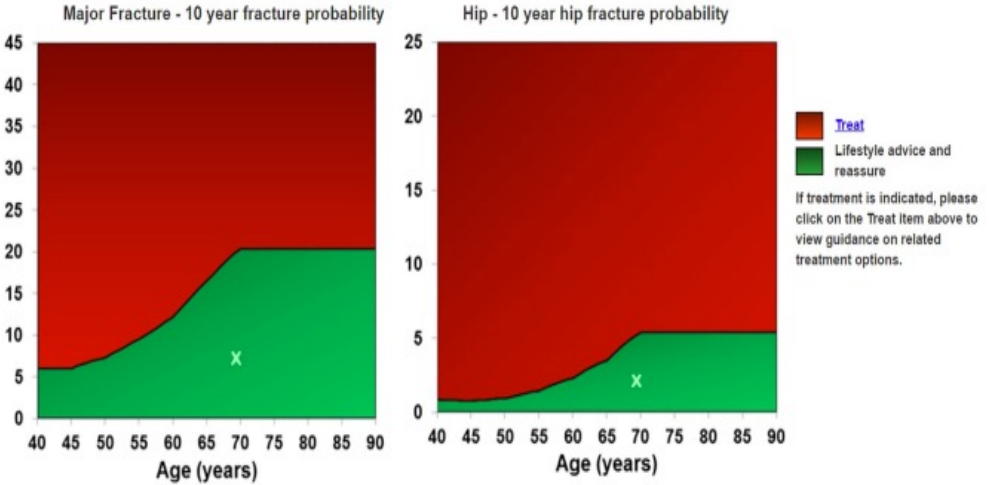
1. Age (between 40 and 90 years) or Date of Birth
   Age: 70 Date of Birth: Y: M: D:
2. Sex: Male / Female
3. Weight (kg): 72
4. Height (cm): 178
5. Previous Fracture: No / Yes
6. Parent Fractured Hip: No / Yes
7. Current Smoking: No / Yes
8. Glucocorticoids: No / Yes
9. Rheumatoid arthritis: No / Yes
10. Secondary osteoporosis: No / Yes
11. Alcohol 3 or more units/day: No / Yes
12. Femoral neck BMD (g/cm²): Select BMD

Clear | Calculate

BMI: 22.7
The ten year probability of fracture (%)
without BMD

Major osteoporotic	8.1
Hip Fracture	2.8

View NOGG Guidance



Guidance for the assessment and management of prostate cancer treatment-induced bone loss. A consensus position statement from an expert group

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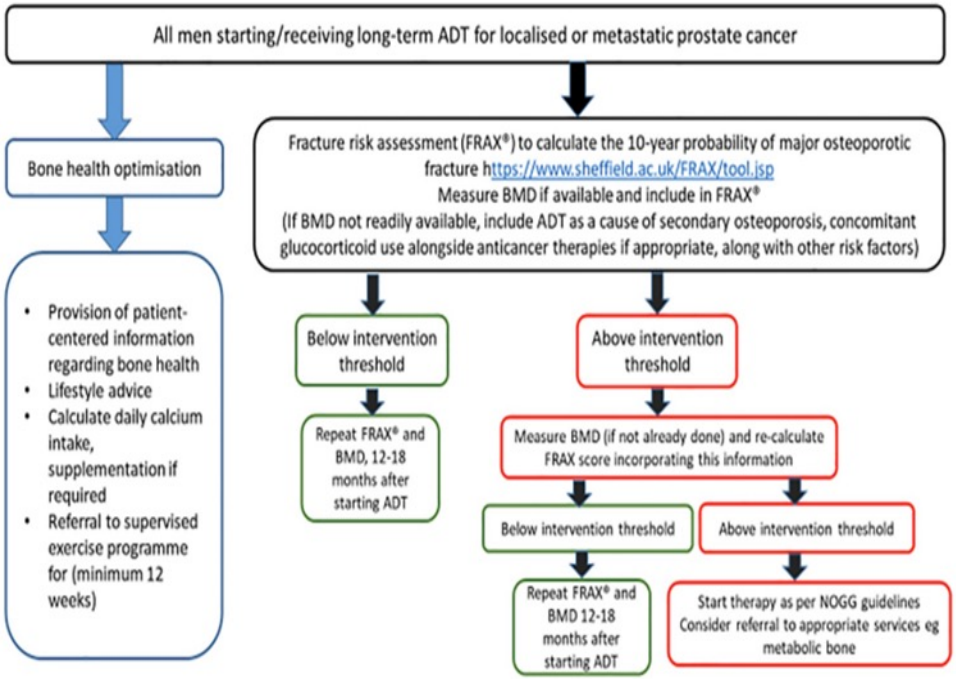
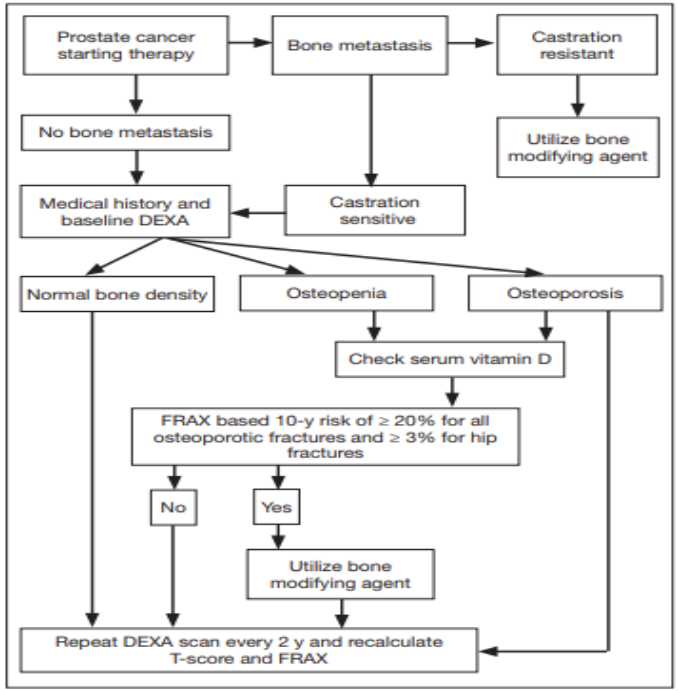


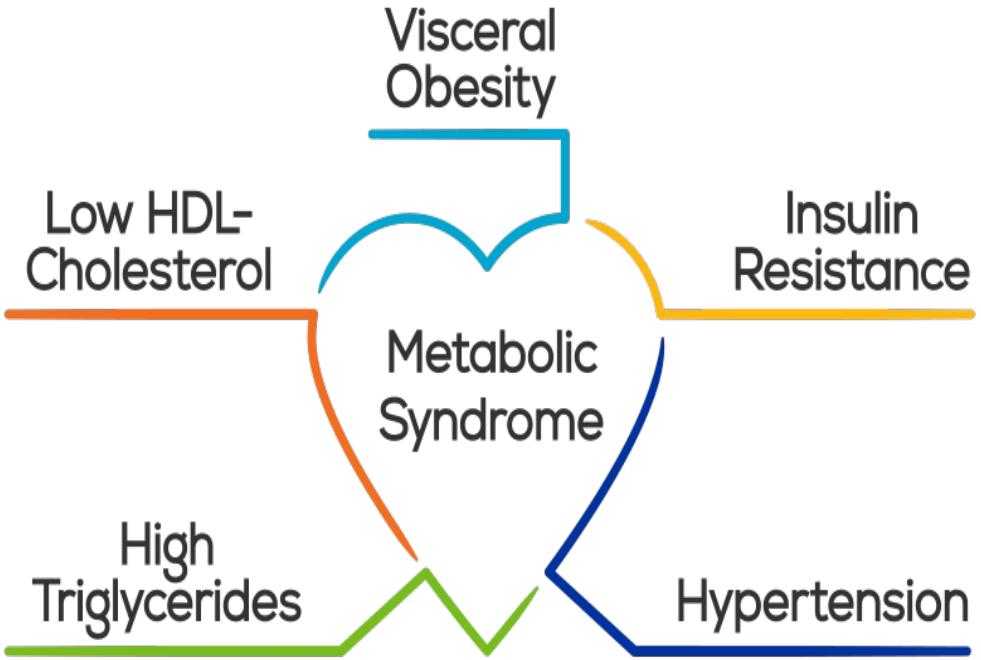
Bone Health in Patients With Prostate Cancer: An Evidence-Based Algorithm

Eric D. Johnson, MD; Katerina Butler, PharmD; and Sumati Gupta, MBBS

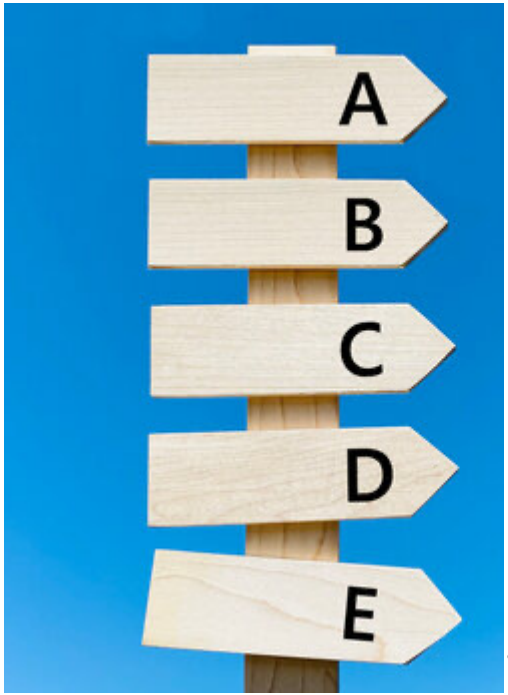


METABOLIC SYNDROME

- Fat mass increases 10-20%
- Lean body mass decreases 2-3%
- Increased insulin levels within months
- Lipids increase in unpredictable ways
- Increases in blood pressure
- Increase in blood sugar levels
- Hemoglobin level could also decline on ADT on average to 125-130g/L (the mechanism is not clearly understood)



METABOLIC SYNDROME: ABCDE Approach



Awareness & Aspirin

- Talk to your doctor about Metabolic Syndrome
- Some patients may need to take Aspirin

Blood Pressure

- Do a baseline blood pressure and regularly during ADT

Cholesterol & Cigarette

- Ask your doctor to check your cholesterol levels
- Decrease or eliminate cigarette use

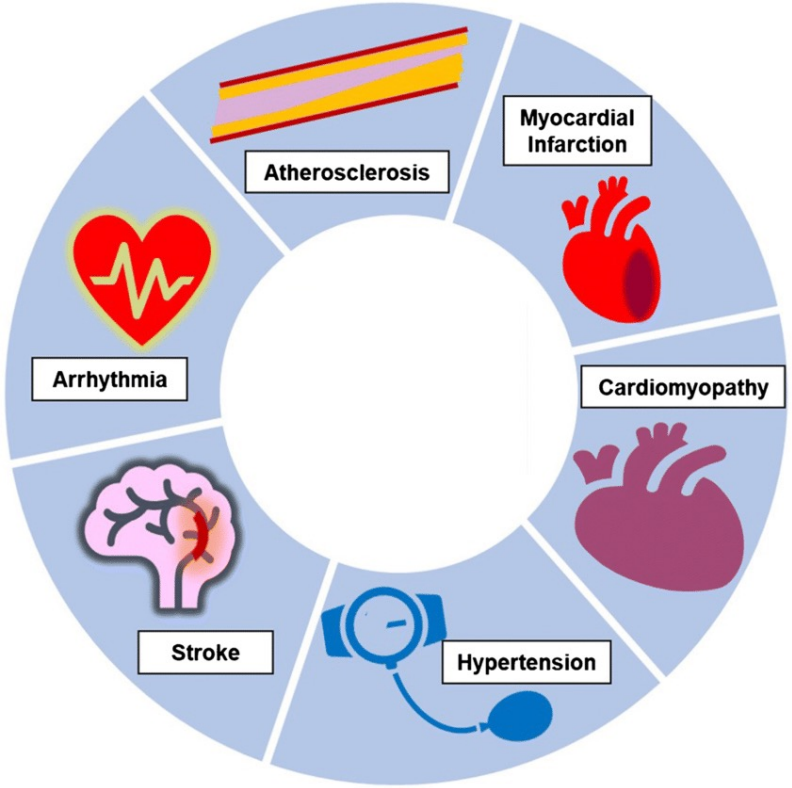
Diet & Diabetes

- Follow a healthy diet and monitor your weight
- Ask your doctor to check your blood sugar levels

Exercise

- 150 minutes per week of moderate-to-vigorous physical activity (aerobic exercise) + 2-3 resistance training sessions

CV DISEASE



Curr Treat Options Cardio Med (2020) 22: 69
DOI 10.1007/s11936-020-00873-3

Cardiovascular Complications of Prostate Cancer Therapy

Summary of AEs/Toxicities with GnRH Agonists and Antagonists

GnRH agonists, compared to antagonists, are associated with:

- Lower impact on libido
- Lower incidence of hot flushes, ED, back pain, weight gain, and constipation
- Lower injection site reactions

GnRH antagonists, compared with agonists, are associated with:

- Significantly lower overall mortality
- Lower CV events

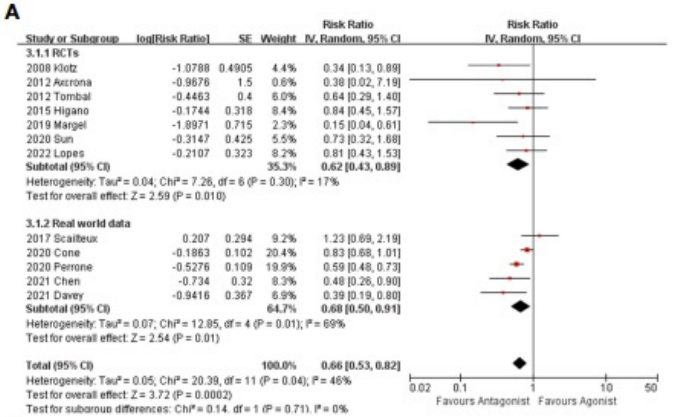
CV DISEASE

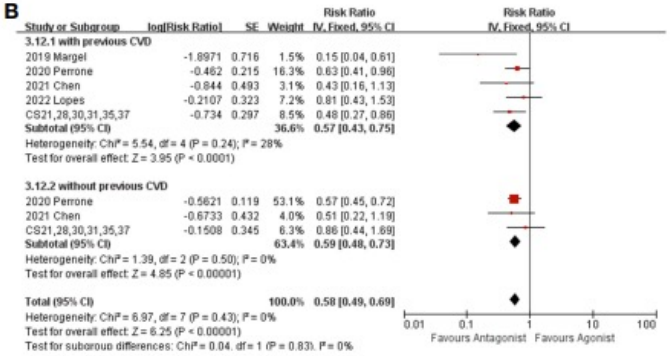
frontiers | Frontiers in Endocrinology

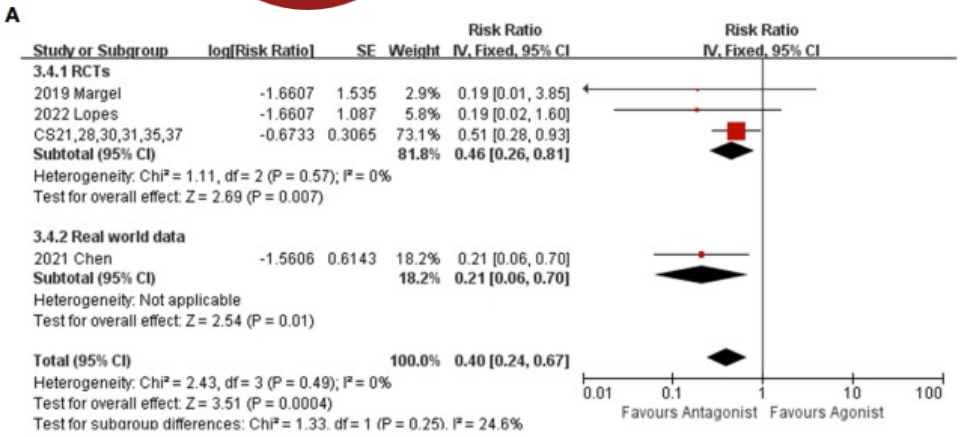
TYPE Systematic Review
PUBLISHED 31 March 2023
DOI 10.3389/fendo.2023.1157857

Adverse cardiovascular effect following gonadotropin-releasing hormone antagonist versus GnRH agonist for prostate cancer treatment: A systematic review and meta-analysis

Li Gu[1], Xurui Li[2] and Wentao Liu[2*]

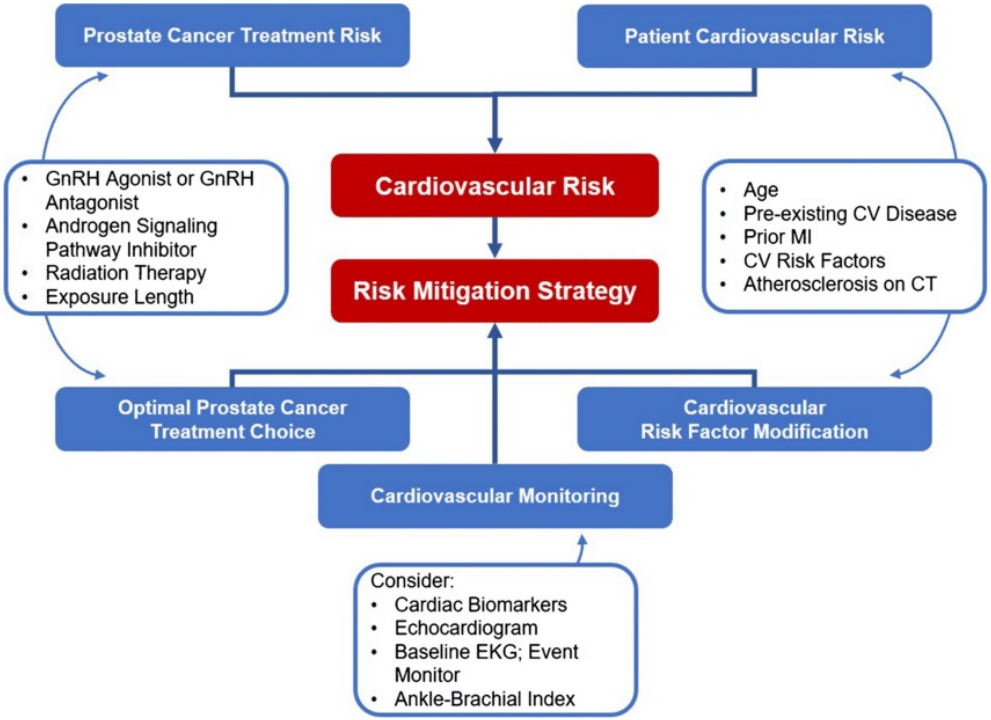






CV DISEASE

- multidisciplinary cardio-oncology team



Cardio-oncology - strategies for management of cancer-therapy related cardiovascular disease

Curr Treat Options Cardio Med (2020) 22: 69
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Cardiovascular Complications of Prostate Cancer Therapy

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Cardiovascular Complications of Prostate Cancer Therapy

TAKE HOME MESSAGES

- ADT can have many side effects
- Up to 20% of men DO NOT have any side effects
- Dealing with side effects proactively is the best way to avoid long term problems with ADT
- Exercise and physical activity are the most effective treatments
- Patients must be active participants in prevention strategies

Grazie dell'attenzione


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AIRO2023

Radioterapia Oncologica:
l'evoluzione al servizio dei pazienti

IL CASO CLINICO

IL PAZIENTE

- 25/08/1948; sposato, no figli, vive con la moglie
- 174 cm, 94 kg (BMI 31)
- Licenza elementare, operaio edile in pensione, vita sedentaria
- Ex fumatore (20 sig/die per 40 anni), vino ai pasti
- LUTS di lieve entità (IPSS: 8), alvo regolare, DE lieve-moderata (IIEF-5: 16)
- No storia chirurgia maggiore
- Nel 2014 STEMI con pPCI. In FU cardiologico
- Comorbidità: artrite psoriasica, dislipidemia, ipertensione.
- Terapia domiciliare: metotrexate + tp steroidea, fibrati, statine, calcio antagonista, clopidogrel

IL PAZIENTE

- 4/2022: riscontro occasionale di PSA totale 6.8 ng/ml
- ER (4/2022): prostata x2, aumento di consistenza a sx
- RM mp (13/05/2022): P5 20 mm mediale lobo sx con associata irregolarità di capsuala, P4 6 mm apice sx, infiltrazione VS sx
- Bio prostatiche (3/6/2022): 12 prelievi random + 3/3 aree target: 8/12 pos GS 4+3 e 4+4, prelievi fusion pos per GS 4+4 e 4+5
- PET Colina di stadiazione (20/07/2022): patologico uptake a carico di prostata e di 2 linfonodi iliaco-otturatori sx, non uptake nodali extraregionali od ossei

STADIO: cT3b N1 M0 iPSA 5.8 ng/ml GS 4+5