Depression and Heart Disease
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- Introduction
- Bible verses
    - Hebrews 13:5 - …I will never leave thee, nor forsake thee.
    - Philippians 2:20 – For I have no man likeminded, who will naturally care for your state.
    - Proverbs 4:20 - 22 – My son, attend to my words; incline thine ear unto my sayings. ..…For they are life unto those that find them, and health to all their flesh.
- Overview
    - Heart disease is the number one cause of death in America.
    - Depression is a risk factor for heart disease (2-fold risk of coronary heart disease with depression).
    - Depression and heart disease are related.
    - Depression is one of the leading causes of disability.
    - Depression is a risk factor for cardiac arrhythmia from increased ANS (autonomic nervous system) activity.
    - Depression is a risk factor for blood clots (↑ platelet aggregation), and MI's (myocardial infarction).
    - Depression is a risk factor for arterioslerotic heart disease (ASHD); ↑C-reactive protein and thus ↑arteriosclerosis; read further for details on interleukin 1, 2, and 6, and TNF (tremor neurosis factor)
    - Depression is a risk factor for cardiac arrest (dysfunction of ANS); 4 fold risk increase of recurrent cardiac events and death with depression.
    - Depression is a risk foactor for myocardial infarction (MI) from ↑inflamatory cystokines and C-reactive proteins.

- Depression is a risk factor for indirect suicide through indirect self-destructive behavior (ISDB):
  - smoking
  - physical inactivity
  - medical noncompliance
- Depression is a risk factor for direct suicide:
  - 35,000 suicides per year in the USA; suicide is the 12th leading cause of death.
  - Indirect suicide through indirect self-destructive behavior (ISDB) causes many more deaths than direct suicide.
- Depression is a risk factor for coronary heart failure (CHF) from neurohormonal activation.
- Depression is a risk factor for coronary heart disease (CHD) at 35% and, CHD is a risk factor for depression; bidirectional activity.
- 20% - 30% of patients with CHF (chronic heart failure) are depressed.
- Depression is a risk factor for ↑cortisol which ↓BDNF (brain derive neurotropic factor), and thus neural death.
- Depression is a risk factor for hyperactivity of hypothalamic-pituitary axis (HPA).
- Depression is a risk factor for adrenal hypertrophy and thus ↑cortisol (adrenal cortex) and ↑NE (adrenal medulla).
- Depression is a risk factor for ↑sympathetic activity and thus, ↑NE (norepinephrine) and thus ↑HR (heart rate) and ↑arrhythmias.
- Depression is a risk factor for ↑weight which ↑CHD.
- Suggestions for Christian patients with depression and CHD:
  - Memorize Bible verses that help in depression, anxiety and anger
    - Hebrews 4:12 – For the word of God is quick, and powerful, and sharper than any twoedged sword, piercing even to the dividing asunder of soul and spirit, and of the

joints and marrow, and is a discerner of the thoughts and intents of the heart.

- Decrease negative intimate relationships (NIRs). A NIR ↑cardiac events by 1/3; work on conflict resolution.
- Decrease stress at job if possible (high demand, low latitude jobs ↑cardiac events).
- Consider SSRIs (Celexa, Lexapro, Zoloft); talk with your medical doctor.
- Decrease stress which ↓inflammation in coronary arteries. Stress is a risk factor for MI (myocardial infarction).
    - Philippians 4:6-8 – Be careful for nothing; but in every thing by prayer and supplication with thanksgiving let your requests be made known unto God. And the peace of God, which passeth all understanding, shall keep your hearts and minds through Christ Jesus. Finally, brethren, whatsoever things are honest, whatsoever things are just, whatsoever things are lovely, whatsoever things are of good report; if there be any praise, think on these things.
- Seek an accountability friend to decrease indirect suicide habits (smoking, low exercise, high cholerterol diet, high triglyceride diet, medical noncompliance)

- Depression and coronary heart disease (CHD) – details
    - Depression is an independent risk factor for CHD.
    - CHD is the leading cause of death and disability in the USA.
    - CHD patients have depression (35%).
    - Thus, there is a bi-directional relationship between CHD and depression.
    - Depression increases all courses of cardiac mortality (MI, CHF, SCD (sudden cardiac death).
    - Depression ↑inflammatory processes.

        - ↑platelet activation → ↑platelet adhesiveness.
        - ↑CRP (Creactive protein) → ↑plaques.
        - ↑interleukin 6
        - ↑tumor necrosis factor (TNF)
    - Psychotherapy did not help according to CREAT (Canadian Cardiac Randomized Evaluation of Antidepressants and Psychotherapy Efficacy) and ENRICHD studies.
    - Psychopharmacology may help (quality of life) according to SAD HART study; ENRICHD said it may ↓risk of death. Considerations from good to not so good include:
        - Citalopram (Celexa), and escitalopram (Lexapro) – low P450 involvement
        - Venlafaxine (Effexor) – low P450 involvement, low anticholinergic side-effects. Can ↑BP at higher doses
        - Zoloft (sertraline)
        - Trazadone (Desyrel) – can ↓BP but overall good drug for many
        - Mirfazapine (Remeron) – can ↓BP and ↑weight
        - Bupropion (Wellbutrin) – overall good but watch BP
        - Duloxetine (Cymbalta) – moderate to potent inhibitor of P450 2D6 80 caution with beta blockers and 1-c antianythmic drugs, also watch BP
        - TCAs – anticholinergic, antiadrenergic, antihistamine effects, sinus tachycardia, tachyarrgythmias, ventricular tachycardia, prolingation of PR, QRS, QT intervals, first, second, and third degree heart block, St-T wave changes
        - MAOI – fatal adrenergic crisis possible
- ASHD (arterioscleretic heart disease) and stress
    - Psychological factors that increase ASHD are:

        - negative intimate relationships (NIR). Those with NIR are 1/3 more likely to have a cardiac event such as a MI or severe chest pain.
        - Job stress – high demand (amount of work and intellectual difficulty) jobs with low latitude (freedom to make decisions) increase cardiac risk.
        - Chronic stress increases inflammation in the coronary arteries resulting in blood clots that cause heart attacks. Chronic stress also increases unhealthy health habits and decreases healthy habits; both increase ASHD.
- Depression and coronary heart disease (CHD)
    - Depression often ↑CHD
    - Depression is linked to ↑weight, ↑DM (diabetes mellitus), and ↑smoking all of which ↑CHD.
    - Depression ↑noncompliance with heart medications and diet which ↑CHD.
    - Depression is associated with a 2-fold increase risk for CHD.
    - Depression, stress, and life events ↑risk of MI (myocardial infarction) more than ↑BP, DM, and obesity.
    - Depression is associated with a 4-fold risk of recurrent cardiac events and death.
    - Depression is associated with ↑5HT2 receptor binding and ↑density of platelet 5HT2 receptors, ↑platelet reactivity, ↑platelet aggregation with ↑thrombus formation; thus, depression and CHD are linked.
- Depression ↑the inflammatory response with:
    - ↑TNF (tumor necrosis factor)
    - ↑interleukin (IL-1, IL-2, IL-6) – proinflammatory cystokines
    - ↑C-reactive protein (CRP)
    - the above inflammatory markers are linked to CHD (CHF or congestive heart failure, ASHD, MI, stroke).

  - Statins ↓Creactive protein (CRP)
- Depression ↑ HPA (hypothalamus, pituitary, adrenal) axis which:
  - ↑CRF or certicotropin releasing factor (hypothalamus)
  - ↑cortisol (adrenal cortex) increased cortisol is associated with CHD
  - ↑catecholamines (NE and E) – catecholamine ↑vasoconstriction and volume expansion in acute state, but chronic vasoconstriction and volume expansion results in CHF.
  - ↑sympathetic activity → ↓parasympathetic activity → ↑CHD → ↑vulnerability to arrhythmia and sudden death.
- Depression – MDD (major depressive disorder) – various details
  - 10% of men will have MDD.
  - 20% of women will have MDD.
  - MDD is usually recurrent.
  - 30% of MDD people have an episode lasting > 2 years.
  - MDD ↑ the morbidity and mortality of:
    - CVD (cardiovascular disease)
    - Chronic pain
    - DM (diabetes mellitus)
    - Respiratory illnesses
  - MDD antidepressant remission rate is 30%.
  - MDD antidepressant response rate is 50%-70%.
  - Discontinuation of antidepressants is due to:
    - sexual dysfunction
    - weight gain
    - perceived lack of efficacy
  - In Star D
    - 30% remission with citalopram 40mg in level 1
    - 70% remaining went to level 2
      - augmentation with bupropion or buspirane =30% response

        - switch to bupropion, venlafaxine, or sertraline =20% response
    - non-remitters in level 2 → level 3
        - augmentation with T3 = 25% remission or $LiCo_3$ = 16% remission
        - switch to nostriptylene =20% remission or mirtazepine = 12% remission
    - Thus, augmentation strategies were more effective than switching.
- Another augmentation strategy to consider is L-methylfolate
    - L-methylfolate is a trimonamine modulator
    - L-methylfolate acts as a regulator of B4 (tetrodrydrobiopterin) important in D and NS synthesis
    - Low serum and red blood cell (RBC) folate levels are associated with ↓ response to antidepressant therapy.
    - L-methylfolate lowers homocysteinel that is associated with depression, dementia, and stroke
    - L-methylfolate helps convert homocysteine to methionine then to SAMe the methydoner of all 3 biogenic amines
- Low serum folate causes include:
    - A genetic polymorphism (C677T – the MTHFR gene) in 50% of the US population; the T/T genotype is in 22% of Hispanic or Mediterranean, 10% of whites, and 70% of depressed patients; the C/T and T/T polymorphisms are less functional forms that result in less L-methylfolate.
    - Poor dietary intake
    - DM (diabetes mellitus)
    - Various GI disorders
    - Hypothyroidism
    - Nicotine dependency

        - Coffee
        - Alcoholism
        - Cigarette smoking
        - Renal failure
        - Medications – lamotrigene, methylpredinosone, sulfasalazine, cholestyromine, colchicines, colestipol, isotretinoin, panalatic enzymes, pentamidine, triamterene, trimethoprin, pyrimethamine, first generation anticonvulsants, oral contraceptives, NSAID for pain, metformin for diabetes, $LiCO_3$
    - L-methylfolate is a cofactor in the synthesis of the monamine neurotransmittors (serotonin, norepinephrine, dopamine).
    - Folate is a water soluble B vitamin (B9); it is one of the 13 essential vitamins: it transfers methyl and formyl groups; it is essential for cell reproduction, the utilization of proteins, the formation of nucleic acids, and several CNS reactions.
- Conclusion
- Bible verses
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