The Head and the Heart: The Association Between Cardiovascular Disease and Depression

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Learning Objectives

• Evaluate existing data in regards to the association between depression and cardiovascular disease
• Describe patient-specific factors to consider when choosing an antidepressant in patients with cardiovascular disease
• Review risks and benefits of utilizing various antidepressant classes in patients with pre-existing cardiovascular disease
• Discuss monitoring of depression symptoms, adverse effects of antidepressants, and monitoring for cardiac adverse effects associated with antidepressants

Introduction

• Cardiovascular disease and depression are both common causes of disability and both can also:
  • Increase medical costs
  • Decrease quality of life
• Over 20 years of data have shown possible increased symptoms of depression following a cardiovascular event
  • May be depressed mood or adjustment disorder vs. “clinical” depression (major depressive disorder (MDD))
  • Non-treatment control groups of depression after an acute coronary event show patient’s mood improves over time
• Is it a “normal” reaction to a stressful life event?
  • Any threat to a person’s well-being or life may be associated with depressed mood
Introduction

- Worse prognosis of CHD in patients with depressive symptoms
- Possible increase morbidity and mortality of CHD
- Decreased adherence to lifestyle modifications
  - Controversial if these changes will have an impact in CHD patients
- Decreased rates of cardiac rehabilitation
- Decreased quality of life

Risk Factors

Traditional Risk Factors which may promote CHD
- Age
- Gender
- Family History of CHD
- Smoking
- Diabetes
- High Cholesterol
- Obesity
- Physical Inactivity

Behaviors seen in depression which may promote CHD
- Inactivity
- Smoking
- Poor diet
- Medication non-adherence
- Social isolation
- Chronic life stress

The Relationship Between CHD and Depression

Potential Biological Mechanisms
- Neurotransmitters
- Inflammation

Potential Behavioral Mechanisms
- Smoking
- Physical Inactivity
- Medication non-adherence

Psychosocial Factors
- Personality
- Anxiety
- History of depression

Demographic Factors
- Age
- Gender
- Social isolation
- Unemployment
- Socioeconomic status
Which came first?

Depression or Cardiovascular Disease

Epidemiology

• Depression
  • Lifetime prevalence of approximately 16%
  • Depression may be a predictor of poor outcome (increased morbidity/mortality) in pts with CHD
    • Including patients with CHD, isolated systolic HTN, post MI, s/p CABG/cardiac valve surgery
  • Cardiovascular death by age 80 (in U.S.)
  • Lifetime risk of 4-7.5% (no CV risk factors)
  • Approximately 20-30% lifetime risk (> 1 CV risk factors)
  • Increased risk of nonfatal and fatal ischemic heart disease after controlling for other risk factors
  • Risk may persist even if depressive episode > 10 years prior to CV event

Epidemiology

• Depression rates
  • Acute MI
    • Some studies say as many as two-thirds of patients may experience mild depression following a MI
    • 15-20% of patients meet criteria for major depression per DSM* criteria
  • CHF
    • Depression rates range from 20-40% seem to increase with severity of illness
  • Following CABG surgery
    • Depression rates range from 15-20%
Epidemiological Studies

• SHEEP study showed MDD requiring hospitalization associated with increased risk of MI
• EPIC-Norfolk United Kingdom Prospective Cohort Study
  • Patients with major depressive disorder (MDD) had 2.7 times higher mortality rates from ischemic heart disease vs. patients without MDD
• Swedish Twin Registry showed risk of developing CAD 2.5-fold higher year after depressive episode and 1.2-fold each subsequent year

Epidemiological Studies

• NHANES 1 study – depression increased risk of mortality from ischemic heart disease independent of HTN
• Majority of trials looking at antidepressant use in CHD:
  • Show improvement in depressed mood
  • May or may not show improvement cardiovascular outcome
  • Some may just show tolerability/adverse effects
• This data supports the hypothesis that depression is an independent risk factor in CHD

Proposed Pathophysiology

Depression Symptoms may cause alterations in the following:

• Platelet clotting cascade
• Heart-rate variability (HRV)
• Autonomic nervous system
• Inflammation
• Endothelial progenitor cell availability
• Hypothalamic-pituitary-adrenal and hypothalamic-pituitary-thyroid axis function
• Myocardial ischemia
• Ventricular instability
• Oxidative stress
• Genetic factors
• Vascular calcification
American Heart Association

The AHA states that although many studies have shown an association between depression and poor outcome in acute coronary syndrome it SHOULD be considered a risk factor for poor prognosis.

Assessment of Depression

• Self-Rating Scales
  • Patient Health Questionnaire (PHQ)-2
    • First 2 questions of PHQ-9
  • If answer "yes" to either question, recommend referral for depression evaluation
    • PHQ-2 and PHQ-9 are tools supported both by American Heart and American Psychiatrist Association as a screening tool
  • PHQ-2 and PHQ-9
  • Patient Health Questionnaire (PHQ)-9
  • Easy tool if patient reporting symptoms of depression in the last 2 weeks
  • Takes minutes to complete

www.phqscreen.com
Assessment of Depression

• Other Rating Scales

  • Beck Depression Inventory (BDI)
    • Self rating scale

  • Hamilton Rating Scale for Depression (HAM-D)
    • Typically used in research
    • Not self-rated

Adjustment Disorder with Depressed Mood

• Occurs as a response to stressful life events (such as acute cardiovascular event)

• Incidence
  • Occurs in as many as half of patients following a cardiac event
  • More common than major depressive disorder

• Treatment
  • Reassurance, social support, education
  • Consider counseling/cognitive behavioral therapy (CBT)
  • Can worsen to MDD
Criteria for Major Depressive Disorder

• Depressed mood or a loss of interest or pleasure in daily activities for ≥ 2 weeks
• Mood is a change from the person’s baseline
• Impaired function in social, occupational, and/or educational areas

*DSM- Diagnostic and Statistical Manual of Mental Disorders

Criteria for Major Depressive Disorder

Greater than 5 of the following symptoms, present nearly every day:

1. Depressed mood or irritable most of the day, nearly every day, as indicated by either subjective report (e.g., feels sad or empty) or observation made by others (e.g., appear tearful).
2. Decreased interest or pleasure in most activities, most of each day.
3. Significant weight change (≥ 5%) or change in appetite.
4. Change in sleep: Insomnia or hypersomnia.
5. Change in activity: Psychomotor agitation or retardation.
6. Fatigue or loss of energy.
7. Guilt or worthlessness: Feelings of worthlessness or excessive or inappropriate guilt.
8. Concentration: Diminished ability to think or concentrate, or more indecisiveness.
9. Suicidality: Thoughts of death or suicide, or has suicide plan.

*DSM- Diagnostic and Statistical Manual of Mental Disorders

The symptoms are not due to the direct physiological effects of a substance (e.g., a drug of abuse, a medication) or a general medical condition (e.g., hypothyroidism).

The symptoms are not better accounted for by bereavement.

Think of the mnemonic: “SIGECAPS”

- Sleep (↑ or ↓)
- Interest (loss of)
- Guilt (inappropriate)
- Energy (decreased)
- Concentration (decreased)
- Appetite (↑ or ↓)
- Psychomotor retardation/agitation
- Suicidal thoughts

*DSM- Diagnostic and Statistical Manual of Mental Disorders
“There are wounds that never show on the body that are deeper and more hurtful than anything that bleeds.”
- Laurell K. Hamilton

Non-pharmacologic therapy

- Self-management of depressed mood
  - Patient education about depression symptoms
  - Behavioral activation
    - Focus attention on pleasant activities
    - Modify negative perceptions
    - Activate social networks
  - Brief counseling if needed
  - Physical activity
    - May improve depression symptoms and cardiovascular health

Non-pharmacologic therapy

- Cardiac rehabilitation
  - Provide services mentioned in self-management strategies
  - Typically provides education and counseling services to help heart patients
    - Increase physical fitness
    - Reduce cardiac symptoms
    - Improve health and reduce the risk of future heart problems

www.heart.org
Non-pharmacologic therapy

• Cognitive Behavioral Therapy (CBT)
  • Safe treatment for cardiac patients who cannot tolerate antidepressants or in mild depression
  • Similar to self-management strategies but can also identify and challenge pessimistic or self-critical thoughts
  • CBT + antidepressants in combination
    • Better than either therapy alone

• Interpersonal therapy
  • Help patients manage interpersonal situations that may contribute to depression symptoms

Pharmacotherapy

• Conflicting data of improved cardiac outcomes with antidepressant use
  • Methodological flaws in studies
  • Unethical to not treat depression (therefore limited studies)
  • Appropriate to treat patients if showing depression symptoms and/or provide support
    • At a minimum, patients will have an improved quality of life
  • Utilize agents with better safety profiles in cardiac patients
    • Consider majority of patients will be elderly
    • Utilize conservative dosing regimens
Pharmacotherapy

- Consider restarting antidepressant that patient had a positive response in the past
- Observe patient closely during first 2 months of antidepressant therapy
  - May take up to 4-6 weeks to see full antidepressant effect
  - Many patients discontinue antidepressants due to side effects or lack of efficacy

SSRI Antidepressants

- Most studied antidepressant class in CHD
- ENRICHD study
  - Non-randomized post hoc analysis of 2481 patients with a recent MI
    - Started on CBT and later randomized to SSRI (or placebo) in 5 weeks
    - SSRI + cognitive behavioral therapy had 42% reduction in death/recurrent MI vs. CBT alone
- Sertraline (Zoloft)
  - Shown to be safe post-MI and/or in CHF patients
  - Should be considered first line as compared to citalopram due to potential cardiac concerns

SSRI Antidepressants

- Citalopram (Celexa)
  - Caution QT prolongation/horseradishes
    - Max recommended dose: 40mg
    - Max recommended dose: 20mg if age > 60 years old, liver impairment, CYP2C19 poor metabolizers, patients taking CYP2C19 inhibitors
  - Caution use in the following:
    - History of QT prolongation, taking other QT-prolonging drugs, bradycardia, recent MI, uncompensated heart failure, > 65 years old, low potassium/magnesium levels
    - Concomitant cytochrome 2C19 inhibitors therapy
      - Omeprazole (Prilosec) and esomeprazole (Nexium); other PPIs, less potent inhibitors
SSRI Antidepressants

- Escitalopram (Lexapro)
  - Thought to have lower risk of cardiovascular adverse effects
  - Max recommended daily dose 20mg
  - Elderly patients: 10mg daily dose

- Adverse effects
  - May increase risk of GI bleeding
  - Potential additive effects from antiplatelet agents (aspirin, clopidogrel) added following a cardiac event

Serotonin Norepinephrine Reuptake Inhibitors (SNRI’s)

- Venlafaxine (Effexor)
- Duloxetine (Cymbalta)
  - May increase heart rate/blood pressure
    - Caution post MI
  - Case reports of worsening heart failure
  - Limited evidence of use in cardiac population
  - Better side effect profile vs. tricyclic antidepressant (TCA)

Other Antidepressants

- Mirtazapine (Remeron)
  - MIND-IT trial: safe and effective in post-MI patients
  - Small sample size, unable to assess all adverse effects
  - May be efficacious in patients with insomnia or those who need to gain weight
  - May cause hypertensive urgency with clonidine
- Bupropion (Wellbutrin)
  - Smoking cessation aid studied in post-MI patients
  - Possible small increases in blood pressure
  - May be activating
  - May increase blood pressure
Other Antidepressants

• Trazodone (Desyrel)
  • Small study showed efficacy in patients with heart disease
  • Case reports of ventricular arrhythmias
  • Often causes orthostatic hypotension
  • More problematic in elderly patients with underlying CHD
  • Adjunctive treatment to another antidepressant for insomnia

• Tricyclic antidepressants
  • Associated with orthostasis, EKG changes, and possibly torsades de pointes
  • Lethal in overdose
  • Avoid post-MI

• Monoamine oxidase inhibitors (MAOI)
  • Avoid due to cardiotoxic adverse effects

• Herbal Supplements
  • St. John’s Wort
    • May potentially interact with other CHD medications
      • Cytochrome P450 3A4 and 2C19 inducers
      • Decreased levels of digoxin, Coumadin, some CCB, some statins
  • SAM-e (S-adenosyl methionine)
    • Less concern of drug interactions
    • Associated with many adverse effects including increased anxiety

Conclusion

• Patients with cardiac disease (both acute events and chronic disease) are more likely to have depressed mood
• Evaluate cardiac patients for symptoms of depression
  • Consider using self-rating scales such as PHQ-2 or PHQ-9
  • Refer patients appropriately who exhibit symptoms of depression
• Non-pharmacologic
  • Encourage active participation in patient’s long-term health
  • Recommend lifestyle modification as well as cardiac rehabilitation
  • Discuss adherence to medications
Conclusion

• Adjustment disorder or mild depression
  • Ensure patients have support they need and/or refer patient for counseling
  • Follow up with patients for potential severity of depressed mood

• Major depressive disorder
  • Cognitive behavioral therapy/other talk therapy in addition to pharmacotherapy have most benefit
  • Consider recommending SSRIs such as sertraline
    • Review patient medications list for drug interactions which may cause additional cardiac adverse effects
    • Ensure patient has adequate follow up especially early in treatment so efficacy and medication tolerability can be assessed

Test Questions

1. The most common form of depression after an acute coronary event is Major Depressive Disorder
   a) True
   b) False

2. What factors should be considered when choosing an antidepressant in patients with cardiac disease
   a) Drug-drug interactions
   b) Potential cardiovascular adverse effects associated with specific antidepressants
   c) All of the above
   d) None of the above
Test Questions

3. One of the safest antidepressants to use in a patient with new onset depression and pre-existing cardiovascular disease (post MI, HTN, CAD) would be:
   a) Venlafaxine (Effexor) XR 225mg PO Daily
   b) Amitriptyline (Elavil) 75mg PO QHS
   c) Citalopram (Celexa) 60mg PO Daily
   d) Sertraline (Zoloft) 200mg PO Daily

4. Which one of the following is not a symptom of Major Depressive Disorder?
   a) Insomnia/Hypersomnia
   b) Decreased concentration
   c) Anxiety
   d) Decreased energy

References