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Cardiac surgery as a stressor and the response of the vulnerable older adult

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Abstract

In an aging population, recovery and restoration of function are critical to maintaining independence. Over the past 50 years, there have been dramatic improvements made in cardiac surgery processes and outcomes that allow for procedures to be performed on an increasingly older population with the goal of improving function. Although improved function is possible, major surgical procedures are associated with substantial stress, which can severely impact outcomes. Past literature has identified that frail patients, who are vulnerable to the stress of surgery, are more likely to have postoperative major adverse cardiac and cerebrovascular events (OR 4.9, 95% confidence interval 1.6, 14.6). The objective of this manuscript is to examine preoperative frailty in biological, psychological, and social domains using cardiac surgery to induce stress. We systematically searched PubMed for keywords including “cardiac surgery, frailty, and aged” in addition to the biological, psychological, and social keywords. In the biological domain, we examine the association of physiological and physical vulnerabilities, as well as, the impact of comorbidities and inflammation on negative surgical outcomes. In the psychological domain, the impact of cognitive impairment, depression, and anxiety as vulnerabilities were examined. In the social domain, social structure, coping, disparities, and addiction as vulnerabilities are described. Importantly, there is substantial overlap in the domains of vulnerability. While frailty research has largely focused on discrete physical vulnerability criteria, a broader definition of frailty demonstrates that vulnerabilities in biological, psychological, and social domains can limit recovery after the stress of cardiac surgery. Identification of vulnerability in these domains can allow better understanding of the risks of cardiac surgery and tailoring of interventions to improve outcomes.

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Keywords

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1. Introduction

Frailty has been defined as a vulnerability to stressors.[1,2] Preoperative frailty predisposes a patient to negative consequences after the stress of surgery. Recent work has identified that frailty is a major risk factor for negative outcomes after cardiac surgery[3-7], with a systematic review demonstrating a five-fold increase in postoperative major adverse cardiac and cerebrovascular events (OR 4.9, 95% confidence interval 1.6, 14.6).[6] While the literature has largely focused on the biological aspects of frailty as a risk factor[8,9], psychological and social frailty can also result in negative postoperative outcomes. This is particularly important in the context of cardiac surgery being offered in an increasingly older and frailer population.[10-13]

Frailty has also been defined as a geriatric syndrome,[14] a broader concept where accumulated deficits[15] on many pathophysiologic pathways can lead to a similar constellation of symptoms (or phenotype). For example, when an older adult suffers femoral fracture following a fall, the phenotype and risk of negative outcomes are clear. However, the cause of the phenotype is multifactorial with the physical environment, sensation, cognition, the emotional state, and social factors all contributing to the fall and fracture. Importantly, focusing on a pre-emptive treatment of a single cause is unlikely to modify the risk (e.g. removing throw rugs does not compensate for reduced muscle strength, poor eyesight, or post-prandial hypotension).[16] Additionally, the literature supporting biological underpinnings is limited with respect to the phenotypic expression of frailty.

Successful surgical correction of cardiac disease has the potential to restore biologic function and provide substantial benefit for older, symptomatic patients.[17,18] However, while many older adult patients survive surgery and return to preoperative functional levels, the perioperative risk of mortality and morbidity from cardiac surgery is higher than in younger patients undergoing similar procedures.[3-7] While the techniques and processes of cardiac surgery have progressed to allow older adult patients to be considered as surgical candidates, the surgery remains a physiological, psychological, and social stressor.[19-21]

Any surgery, including cardiac surgery, is a stressor to the patient. This manuscript examines frailty by using cardiac surgery as a “stressor” event in the older adult population. A vulnerable patient, who is more susceptible to the complexity of surgical process, will be at-risk for complications of the surgery and will be less likely to return to function postoperatively (Figure 1). The process of cardiac surgery is typically very structured: a) there is a baseline assessment; b) the surgical procedure (i.e. stressor) most commonly occurs a predetermined time and place; c) there is measurable systemic response; and d) there is anticipated survival and recovery course. (Box 1 describes stressors associated with Cardiac Surgery). By expanding the scope of vulnerability within the construct of the biopsychosocial model after cardiac surgery, we acknowledge that the surgical process

includes factors that are outside of the control of the peri-operative team and may influence outcomes.

1.1 The Biopsychosocial Model and Frailty

This Biopsychosocial Model has been applied in multiple conditions to understand the impact of illness[22], particularly complex diseases. The syndrome of frailty has been applied to the Biopsychosocial Model using the stressor of cardiac surgery in this review. In the biological, psychological, and social domains, the literature supports frailty as a vulnerability to the stress of cardiac surgery. In the following sections, the association of frailty in each of the biopsychosocial domains with negative health outcomes after cardiac surgery will be reviewed. Importantly, there is a substantial overlap among the domains. For example, cognitive frailty has biological, psychological, and social underpinnings that contribute to negative outcomes after surgery. Describing the overlap of domains is not possible within the scope of this manuscript.

1.2 Age, Vulnerability, and Frailty

One of the critical areas of overlap – age deserves mention. Age is inextricably linked to frailty, but not causally related.[14,23] In the case presented, the patient's age is a risk factor for perioperative morbidity and mortality. However, the acuity of the patient's cardiac illness[24], physiology as well as the underlying comorbid disease[25] and functional[24] status, should be considered in the decision for cardiac surgery. Chronological age alone cannot be the sole factor in determining operative vulnerability.

2. Biological Frailty

2.1 Case Continued

Mr P. has many chronic medical conditions including hypertension, hyperlipidemia, benign prostatic hypertrophy, osteoarthritis of the knees and hands, gastroesophageal reflux, and constipation. He takes 8 different medications and a multivitamin every day. He is able to walk about 100 meters before the chest pain causes him to stop. Mr P. develops chest pain during the climbing of one flight of stairs to his bedroom. He frequently complains of fatigue and takes an afternoon nap daily. He has had an unintentional 4-kilogram weight loss in the 12 months.

When considering the biological domain, there is a significant body of evidence that the contribution of physiological function[26,27], comorbidity[27,28], and inflammation[29,30] contribute to a patient's vulnerability for negative outcomes after cardiac surgery.[31] The case presented identifies multiple comorbid conditions and treatments, each with a molecular underpinning that can contribute to a negative response to stress. For example, the osteoarthritis of the knees, in addition to limited mobility, is associated with an increase in baseline inflammation and subsequently treated with an agent (nonsteroidal anti-inflammatory drugs) that affects platelet function thereby increasing the risk for bleeding after surgery. Each factor has a separate biological underpinning and cumulatively contributes to a propensity for adverse events after cardiac surgery, yet each is dependent on the others.

2.2 Physiological frailty

There are, presently, two major scoring systems that are commonly utilized to predict the risk of negative outcomes following cardiac surgery. Both the Society of Thoracic Surgeons (STS)[27,32] and the European System for Cardiac Operative Risk Evaluation II [26] (EuroSCORE II) risk prediction tools are sophisticated models used for prediction of morbidity and mortality following cardiac surgery. As a result, the physiological variables entered into the models meet the broad definition of frailty. While these tools have incorporated age, both in their current iteration, focus on “traditional” physiology variables and thus provide information limited to the patient's physiological vulnerability. It is becoming increasing evident that a more comprehensive assessment that involves the psychological and social frailty assessments as part of their algorithm is necessary for the contemporary cardiac surgery patient.[4,33]

2.3 Comorbidities

On a fundamental level, medical conditions reduce an organ system's ability to respond to stressors and multiple comorbidities should increase vulnerability to the stress of cardiac surgery.[34] While both the STS and EuroSCORE II risk prediction scores incorporate a collection of co-morbid disease, listing diseases provides a basic measure of organ function and does not account for the range in organ function. Additionally, many chronic medical conditions such as inflammatory, cognitive, or oncologic conditions are not included as these are not presently routinely collected as part of the preoperative evaluation as the majority of currently utilized assessments did not consider the aging population that is now being referred for cardiac surgery procedures. Therefore, as the incidence of comorbid medical conditions grows in an older and complex operative population, there is a need to have a deeper understanding how the additional factors increase a patient's vulnerability to the anticipated stress of their surgical procedure. Past work identified that comorbidity was a risk factor for frailty.[35] With increasing comorbidities, comes increased preoperative medication utilization and potentially altered drug metabolism.[36] The potential for interactions, reactions, and adverse events increases when baseline polypharmacy is combined with the perioperative medications.[37]

2.3 Inflammation

In studies of sepsis[38], trauma[39], surgical complications[40], and exercise[41], those patients with higher baseline circulating inflammatory cytokines had an heightened and prolonged inflammatory response compared to those with lower baseline inflammation. Importantly, preoperative levels of inflammatory markers have been shown to be higher in frail versus non-frail individuals, [35] and has suggested that chronic low-level inflammation makes one prone to frailty.[42,43] During cardiac surgery, there is a dramatic rise in inflammatory markers with levels that can be over 100 times the baseline level.[40,44] Therefore, when primed with pre-existing low level inflammation, the response to stressors following cardiopulmonary bypass can be significantly amplified.[45,46] As a result, frail patients with low levels of inflammation may have more of an inflammatory response which might contribute to negative postoperative outcomes such as vasoplegia, atrial fibrillation and delirium.[47,48]

2.4 Physical Frailty

With the description of Fried's Frailty Phenotype[35], there is a growing body of literature on the interrelationship of physical frailty and multiple negative consequences. Fundamentally, this physical frailty model can be utilized to further our understanding of responses to the stress of cardiac surgery. In the sections below, we examine the components of this frailty phenotype with relationship to cardiac surgery stress.

2.4.1 Decreased activity—The presence of underlying chronic disease further contributes to the limitation of physical activities in older adults, leading to acceleration of catabolic process.[49,50] Importantly, preoperative gait speed is developing as a marker of morbidity and mortality after cardiac surgery.[51] In the case outlined above, the presence limits of preoperative physical activity combined with osteoarthritis, hormonal imbalance/ deficiency such as testosterone imbalance, compounds the problem. Instrumental activities of daily living (IADLs) dependence and the use of walking device were independent predictors of the outcome of cardiac surgery in the older patients.[52]

2.4.2 Sarcopenia—Sarcopenia, a loss of muscle mass, is associated with adverse clinical outcome after cardiac surgery.[53] The loss of muscle mass associated with sarcopenia represents not only a risk in physical capabilities for recovery, but an unknown impact on cardiac muscle function. In a healthy older adult population, the loss of 70% of basal muscle power was associated with physical frailty.[54]

2.4.3 Weight loss—There are extremes of weight that can lead to vulnerability after cardiac surgery. Both malnutrition from protein deficiency and obesity are associated with poor wound healing and multiple complications[55] and low albumin associated with operative mortality.[56] Further complicating the picture are dietary restrictions[57], difficulties in chewing and swallowing[58], medication and their side effects[37], and comorbidities.[34] Importantly, the value of weight loss is a marker of morbidity and mortality after cardiac surgery.[59]

2.4.4 Exhaustion—Exhaustion was the defining feature of frailty in patients with CVD.[3] In combination with the psychological domain below, the exhaustion component represents the overlap of physical and psychological frailty.

3. Psychological Frailty

3.1 Case Continued

Mr. P had difficulty maintaining the house after the death of his wife 2 years ago as she managed many of the household activities. Currently, he drives to the store, prepares his meals, and is able to perform housework. He depends on his neighbors for maintaining the exterior of his home which the chest pain has proven limiting. He is frustrated by the physical limitations, but thankful that he is able to continue driving. He states that he has no problems with memory besides forgetting where he put his keys. He denies having symptoms of depression.

The relationship between atherosclerosis and psychological disease, including cognitive impairments[60,61] and psychiatric disease[62], has been well established. We used the psychological domain of frailty to examine how the stressor of cardiac surgery impacts the recovery. While psychological frailty lacks the definitive criteria and measurement ability of physical frailty, few would argue that recovery in the psychological domain is critical to returning to preoperative levels of function.[63,64]

3.2 Cognitive Frailty

The impact of cardiac surgery on postoperative cognitive function has been debated for years.[65,66] Challenged by measurement of cognition before and after cardiac surgery[65,67], there are some fundamental vulnerabilities that may predispose patients to subsequent cognitive decline. It needs to be stated clearly that most patients who undergo cardiac surgery return to baseline.[68,69] However, a small group of patients have a measureable cognitive decline after cardiac surgery.[68-70]

3.2.1 Preoperative Cognitive impairment—Patients with atherosclerosis have lower preoperative cognitive performance.[69] There are many studies which identify a fundamental cognitive decline preoperatively in those patients undergoing cardiac surgery relative to age, gender, and education matched controls.[69] If a cognitive insult is associated with cardiac surgery, those with pre-existing cognitive impairment are more likely to experience further decline.

3.2.2 Delirium—Delirium is an acute change in attention and cognition that occurs in up to 50% of cardiac surgery patients.[71] Delirium is independently associated with functional decline after cardiac surgery.[72] Recovery in surgical patients with delirium can be delayed, particularly in those patients with preoperative cognitive impairment.[73] Patients who are preoperatively frail are more likely to develop delirium.[74]

3.2.3 Postoperative Cognitive Decline—While measurement of cognitive function is challenging in the preoperative and postoperative settings, there are several comprehensive reviews of cognitive decline following cardiac surgery.[66,67] This postoperative cognitive decline has been found in both cardiac[68-70] and non-cardiac surgery[75,76] and can last for years. Postoperative cognitive decline appears to be more common among those with pre-existing cognitive impairments, however, suggesting that the decreased cognitive reserve is unable to respond to the stress of the surgical procedure (Figure 1).[77]

3.3 Mental Health

3.3.1 Depression—Cardiac surgery is associated with mental health stress when measured on standardized questionnaires. Rating questions regarding energy, mood, appetite, and thoughts about the future are contextually different as a patient is adapting to the impending cardiac surgery. A systematic review found that as patients entered the recovery period (2 weeks postoperatively), depressive symptoms measured on standard instruments and depression diagnosis was lower than preoperative levels.[78] Importantly, those who were diagnosed with depression more than 1 week prior to cardiac surgery were

less likely to experience depression remission postoperatively.[78] This response to the mental health stress of cardiac surgery can provide valuable insight into cardiac surgery outcomes.

Despite the timing limitations, screening for preoperative depression has been found to be an important determinant of outcomes following cardiac surgery. Cardiac events included angina or heart failure that needed admission to hospital, myocardial infarction, cardiac arrest, percutaneous transluminal coronary angioplasty, repeat CABG, and cardiac mortality.[79] There remains considerable debate as to whether depression in itself is a vascular phenomenon related to the atherosclerosis in these patients.[62] The clinical take away highlights the importance of screening for depression in both pre- and postoperatively setting.[63,64].

4. Social Frailty

4.1. Case Continued

Mr. P has lived in the same town for over 60 years and was once very connected in civic and religious organizations. He has seen his social network decline due to deaths and functional limitations of his friends. He feels less connected and does not regularly attend services. He has three children and four grandchildren. His daughter lives 45 minutes away, however tries to visit weekly. His other children and grandchildren live in distant states. He draws a small pension and has social security for income which allow him to pay the bills without savings. He recently asked his daughter to assist with paying the bills after a recent hospitalization.

There are social factors that predict recovery after cardiac surgery such as adaptive characteristics, social support, geographic distance, and socioeconomic status. There are also gender[80] and racial disparities[10]in the availability of cardiac surgery care that influence outcomes. Additionally, sociodemographic influences can impair cardiac surgery outcomes. For example, <12 years of education increases risk of long-term mortality after cardiac surgery.[81] These factors appear to be independent to the biological, physical, and cognitive stress of cardiac surgery.

4.2. Coping

While cardiac surgical care and outcomes continue to improve[10], cardiac surgery brings a substantial “unknown”, particularly for the under-informed patient. For example, a cardiac surgery patient is subjected to perioperative protocols for pain, ambulation, and nutrition. These protocols are appropriate for care, but can be different from the patient routine. While most patients will adapt to the short-term change in routine, frail patients have been described to have a maladaptive response to such stressors.[82] Similarly, increased anxiety measured preoperatively has been associated with negative outcomes postoperatively.[81]

Coping with these risks and deviations from routine, draw on the patient's psychological and social functioning. For example, older hospitalized, patients who have low psychosocial resources had increased hospital mortality, longer LOS, discharge to a higher level of care, and increased readmission.[52] Additionally, short-term depression and anxiety among older adults following cardiac surgery are partially alleviated when patients employ prayer and are hopeful as part of their coping strategy, but may not impact long-term outcomes.[83]

4.3 Social Support

Postoperative recovery following cardiac surgery draws on the patient's social structure.[84] For example, having home support for daily activities, such as driving to follow up appointments, allows a patient to focus on recovery. A recent report found that married patients had improved mortality or functional recovery relative to separated or widowed patients.[85] Social support might allow home-based cardiac rehabilitation which was associated with improved health related quality of life[86] relative to usual care. Another study found that patients who lived near the hospital where surgery was performed had lower mortality, presumable due to the ability of social support during and after the surgery.[87]

4.4 Addiction

In addition, preoperative addiction can be a risk factor for negative surgical outcomes. Pain perception is different in patients with nicotine and opioid addiction. Preoperative alcohol intake is associated with increased complications.[88] Smokers were noted to have higher amount of pain medication after CABG compared to non-smokers.[89] Routine use of nicotine replacement therapy is not recommended as a randomized study found increased mortality after CABG[90] and a meta-analysis of ICU patients was not conclusive.[91] Patients with opium dependence have a high threshold for pain medication and a recent study showed that spinal anesthesia may reduce the incidence of postoperative delirium.[92]

5. Overlap of Biopsychosocial Frailty Domains

5.1 Case Continued

Mr P. and his surgeon have a discussion about cardiac surgery including the perioperative course, the need for follow-up and cardiac risk modification, the potential benefits to his function, and the potential operative, functional, and cognitive risks. In evaluating the patient, the surgeon collects information on the patient's baseline physiologic function, his limited physical performance, his cognitive decline, and his social isolation. The patient wants to discuss the surgery with his daughter before deciding to undergo surgery, as the decision would affect her as well.

5.2 Overlap

In the context of the cardiac surgery stressor, there are vulnerabilities within the biological, psychological, and social singular domains alone that influence poor recovery. Pragmatically, these vulnerabilities do not occur within the isolation of a single domain – there is overlap. For example, increasing age is associated with comorbidity, physical frailty, cognitive impairment, depression, social isolation, socioeconomic status. All of these factors are independently associated with outcomes after cardiac surgery. Logically, we assume that the accumulation of deficits in a cognitively impaired, highly-comorbid, and isolated patient is going to present a less optimal candidate for surgery. However, the intersection of these domains with cardiac surgery outcomes needs exploration to make this definitive statement.

6. Conclusion

With the acceptance that cardiac surgery is a stressor event for the older adult patient, the recovery response following surgery can be utilized to gain an understanding of a population who might not be able to recover from that stress – a frail population. Frailty is a geriatric syndrome[14,93] with a constellation of symptoms and many contributing factors. While literature has primarily focused on physical frailty, vulnerability in the psychological or social domain contributes to the vulnerability to the surgical stressor. Deficits in multiple domains likely increase the risk of negative postoperative outcomes. Lastly, despite choosing a focus on cardiac surgery, the literature on the impact of perioperative frailty remains sufficiently heterogeneous. As such this review serves to highlight the need for standardized definitions and measurement tools in older adult undergoing surgery. Preoperative screening is helpful at identifying vulnerabilities, but the clinically applicable tools for this screening need additional prospective clinical investigation.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Clinical Vignette

Mr. P is 86 year old man develops typical crushing chest pain with exertion that does not respond to medical therapy. On non-invasive testing he is found to have ischemia with mild activity and a large reversible defect. Catheterization demonstrates three-vessel coronary disease and he is scheduled for cardiac surgery.

Box 1

Stressors of Cardiac Surgery

- Biological
  - Inflammation
  - Anaesthesia
  - Fluid Shifts
  - Cardiopulmonary Bypass
  - Pain
  - Immobilization
  - Sleep Deprivation
- Psychological
  - Cognition
  - Depression
  - Anxiety
  - Delirium
  - Self-perception
- Social
  - Physical limitations
  - Care demands on family
  - Financial resources
  - Access to necessities
  - Community isolation
  - Threats to independence

Highlights

- Cardiac surgery is a stressful event in the life of an older patient
- Recovery from cardiac surgery is dependent on the vulnerabilities of the patient
- Vulnerabilities to the surgery occur in biological, psychological and social domains
- Overlap of vulnerability domains likely increases the risk of negative outcomes

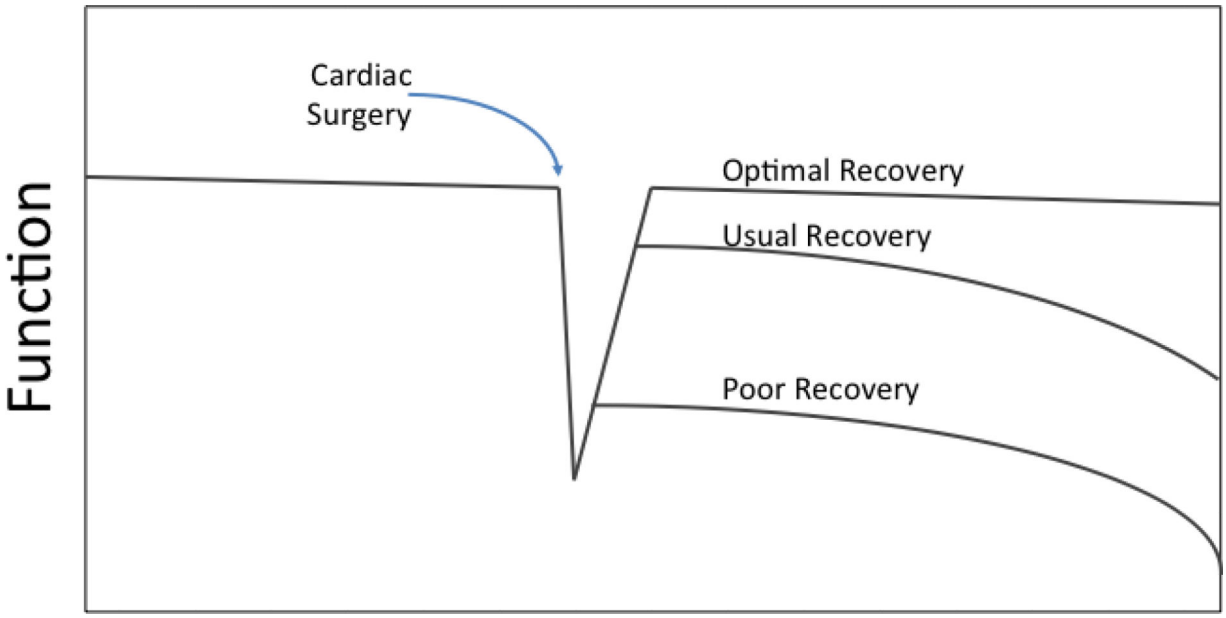

Figure 1. Response to Stressors

When a frail patient is subjected to a stressor, such as cardiac surgery, there is a reduced ability to return to the prior level of functioning and frequently negative outcomes. They tend to attend a new “baseline”. As these stressors become more severe or more often, the baseline status continues to trend down. Patients with pre-existing vulnerabilities may undergo cardiac surgery at lower functional levels (i.e. cardiac surgery stress is shifted right).

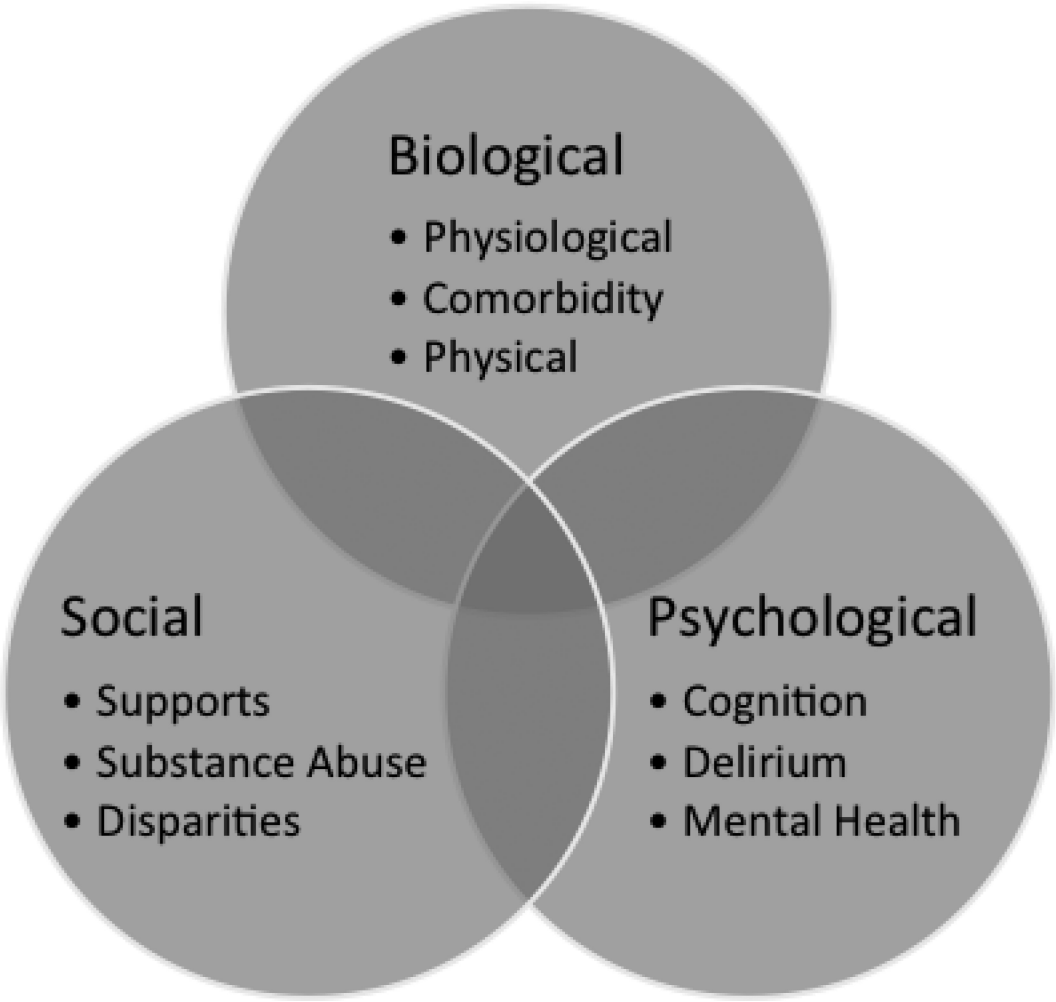

Figure 2. Biopsychosocial Model for Frailty

As a vulnerability to stress, frailty can occur in the biological, psychological, or social domains. Importantly, there is overlap among the domains, resulting in vulnerability outside of the narrowly defined physical frailty criteria.