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Review

Surgical resilience: A review of resilience biomarkers and surgical recovery

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ABSTRACT

Background: Two distinct and large bodies of literature exist on resilience that are of potential interest for surgical outcomes. First is the literature on the impact of resilience on surgical recovery and wound-healing. Second is the literature on biomarkers for resilience, which largely focuses on neuropeptide Y (NPY), testosterone and dehydroepiandrosterone (DHEA). Despite this activity, there is a dearth of literature linking these two bodies of research by investigating biomarkers for surgical resilience and its impact on surgical recovery. This paper reviews both bodies of literature within the context of surgical recovery.
Method: Literature searches within Medline and Embase were conducted for studies and previous reviews of resilience biomarkers and for the impact of individual resilience on surgical recovery. Reference lists of the reviews were searched for additional papers. No systematic review is yet possible due to the novelty of the use of resilience biomarkers within a surgical context.
Results: This is the first review to explore a potential link between resilience biomarkers and surgical recovery. There are a number of biomarkers that correlate with individual resilience levels and resilient individuals exhibit better recovery trajectories following surgery, suggesting a novel use of such biomarkers for the identification of "surgical resilience".
Conclusion: By identifying surgical resilience, there is potential for utilising these biomarkers as prognostic indicators of likely recovery trajectories from surgery, which in turn complement individualised peri-operative management.

Introduction

Surgery is a stressful experience, both physiologically and psychologically. The pre-operative assessment of the patient's age, their physical condition, co-morbidities and nutritional status is the current standard of care in order to prevent many complications and their sequelae.[1,2] Indeed, sufficient time prior to elective surgery can enable modifiable

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risk factors to be addressed. For instance, it is well known that low levels of pre-surgery fitness greatly increase the risk of complications and recovery duration.[3–5] Improving patient pre-operative fitness – or prehabilitation, as coined by Ditmyer and Topp – has been advanced as a preventative measure.[6,7] The effectiveness of such prehabilitation is evident, though patient adherence can be an issue.[8] The effects of pre-surgery fitness are not only physiological, but help to reduce psychological stress.[9]

The pathophysiological response to surgery has been widely investigated in the systemic response to injury and metabolic support. This response encompasses a complex inflammatory, central nervous system, endocrine and cellular interaction during the different phases which in turn will determine a successful wound healing and eventual recovery.

The complexity of the response has been monitored with an extensive biomarker repertoire and while surgical wound healing lends itself to a number of cytokine biomarkers including IL-1α, IL-8 and TGF-α which are all readily measurable and specific to wound healing in the epidermis.[10] Within the surgical recovery setting, the biomarker repertoire is greater still. Complications encountered during cardiac surgery, such as acute kidney injury and neurologic injury, have readily available biomarkers[11–14] as do outcomes for patients requiring extracorporeal life support following cardiac surgery.[15] Prognostic biomarkers have been explored for age, diabetes and nutrition.[1] While wound healing physiology is stereotypical, it is moderated by these factors, which have their own prognostic biomarkers for recovery.

The duration of the pathophysiological response to surgery is variable, ranging from days to months.[16] Janis speculated that individual variability points to psychosomatic dimensions, but his early theoretical work lacked clinical trials.[17] More recent systematic reviews and meta-analyses lend support to Janis's view by showing there is a probably a psychological effect on surgical recovery.[10,16,18] There is some evidence of a relationship between patient preoperative state anxiety and perioperative mood and pain,[16] and there is strong evidence of an association between state anxiety and wound healing.[10] The evidence supports a psychological mediation of postoperative recovery, but not all individuals experience the same levels of anxiety. As observed by Janis, it may be reasonable to assume the contextual stimulus is consistent for a given operation, but one can observe a high variability in individual responses to that stimulus.[17] Some patients are more "resilient" and exhibit a lower response to stress than others.[16,17] As this current review considers "resilience" within a surgical setting, the phrase "surgical resilience" will be used with that meaning.

It should be noted that there are mixed results on any potential correlation between stress biomarkers and surgical recovery.[19,20] Without a clear correlation, the question of whether a causal relationship between stress biomarkers and surgical recovery is inconclusive and further research is demanded. Consider this: if there is a psychological mediation of postoperative recovery, and if the results of stress biomarkers are inconclusive, then one may reasonably argue that individual surgical resilience plays a larger role in the psychological mediation of recovery by virtue of the fact that resilient individuals exhibit a lower stress reactivity than non-resilient individuals. Within the context of biomarkers, one could reasonably hypothesise thus: if a resilience biomarker is present, then a patient will be likely to have a shorter recovery. Yet no research exists in Medline or Embase on any such correlation between resilience biomarkers and surgical recovery, despite the large body of research on resilience biomarkers and the large body of research on the role of resilience in surgical recovery. Indeed, of the two large bodies of research, there are only two papers that overlap both topics, neither of which explore the possibility of a link between the two bodies of research.[21,22] This effectively rules out the possibility of conducting a systematic review. Exploring the measurability of resilience biomarkers in order to provide individualised management of the surgical patient is the aim of this review. This leads towards a new concept of surgical resilience and the use of resilience biomarkers to complement the peri-operative management of patients.

What is resilience?

Within the biological context ecological resilience is the ability of an ecosystem to maintain its normal patterns of nutrient ecology and biomass production after being subjected to damage caused by an ecological disturbance.[23] In the medical context it is an ability to recover from or adjust to misfortune or change.[24] Psychological resilience is characterised by the ability to accept circumstances that cannot be changed and adapt to significant changes in the environment.[25–30] As such it is intimately related to stress and state anxiety. Stress represents an interaction between the individual and the environment in which the demands of the situation are perceived as exceeding the resources of the individual.[27] Resilient individuals have diminished stress reactivity and better emotional recovery than individuals who are less resilient.[31] Importantly, resilience is protective against state and trait anxiety and anxiety disorders.[32,33] It is essentially a "psychological shock absorber"[26] or a "homeostatic return to a prior condition" following an adverse effect.[34] Carver illustrates the concept of resilience, comparing it with other possibilities (namely "survival with impairment" and "succumbing"),[34] as shown in Fig. 1.

What psychological factors could account for these differences? Consider the examination of the psychological process of resilience within a "broaden and build" theory of emotions.[29] According to this theory, positive and negative emotions have complementary adaptive functions and effects: negative emotions narrow one's perspective of a situation and prepare one to act in a specific way; positive emotions allow one to broaden one's perspective and grow from the situation, stressful or otherwise.[35] Resilient individuals tend to utilise positive emotions to regulate stressful experiences and to find meaning within and grow from the experience.[29] Other psychosocial factors that encourage resilience through the cultivation of positive emotions include having purpose, social and family support and optimism[31,36,37]; findings that indicate resilience may be able to be bolstered. Indeed, it can be trained into one's psychology, allowing the individual to "bounce back" quicker than before.[25,33,38–41]