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Literature Review

Postoperative Depression: Insight, Screening, Diagnosis, and Treatment of Choice

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Abstracts

Introduction: Postoperative depression is a condition of depressive effects in patients without symptoms of depressive mood that occurs a few weeks after surgery and persists for at least 2 weeks. It generally possesses the same symptoms as major depressive disorder. **Review:** Their difference is that surgery is the trigger of depression in postoperative depression cases. Postoperative depression is associated with increased patients' morbidity and mortality, increased the risk of disease complications, reduced postoperative healing process, prolonged the duration of treatment, and reduced patients' quality of life. Therefore, mental health conditions should always be assessed on patients after undergoing surgery. Postoperative depression therapy needs to consider the benefits of antidepressants and adequate pain management. Antidepressant considerations also need to consider interactions with other drugs. Psychotherapy and cognitive behavioral therapy are also useful in postoperative depression management. **Conclusion:** This review is aimed to give insight about postoperative depression, its importance, and how to treat it.

Keywords: Postoperative Depression, Insight, Screening, Diagnosis, Health Risk

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INTRODUCTION

Postoperative depression is a depression episode that develops after surgery in people with no prior symptoms of depression. It generally possesses the same symptoms as major depressive disorder. Their difference is that surgery is the trigger of depression in postoperative depression cases [1]. Postoperative depression may be caused by a defense mechanism of physiological disruption, chronic pain, and distress. Postoperative delayed paradoxical depression is a psychiatric condition where major depressive disorder occurs weeks (hence the name "delayed") after successful, uncomplicated surgery. Postoperative depression is not always caused by failure in the surgery, but it can also happen in successful surgery procedures, which is known as postoperative delayed paradoxical depression. Since postoperative depression may develop weeks after surgery, it is also regarded as a variation of post-traumatic stress disorder (1, 2, 3). Postoperative depression is often related to postoperative acute pain or inadequately treated chronic pain. It is also related to surgery-induced immunosuppression. Physiologic stress and depression worsen each other's conditions [1]. The rate of postoperative depression is around 21-50% [5]. New-onset postoperative depression is a depression episode occurring soon after a surgery is done in which the patients have no prior history of depressive mood. Postoperative delayed paradoxical depression is not a transient mood disorder or minor depressive mood. Postoperative delayed paradoxical depression is a major condition that may hinder recovery. It is called "paradox" because it happens to patients who should be feeling relieved after a successful surgery, but they feel depressed instead. It is often regarded as a mild variation of post-traumatic stress disorder. Depression in general is the most frequent mental illness and is one of the leading causes of productivity decrease [6]. Postoperative delayed paradoxical depression was first identified by Richard Blacher in 1978 after observing a lot of depression cases in patients after successful cardiovascular surgeries (3). Postoperative depression has been documented to occur in various kinds of surgeries. It has occurred in the Coronary Artery Bypass Graft procedure [7]. It has also been reported after spinal [8] and arthroplasty [9] surgeries. Postoperative depression was also documented in surgeries for treatment of various types of cancer [10–12].

Postoperative depression is related to increased morbidity and mortality, increased risks of complications, prolonged length of stay, and dereased quality of life [1]. It also triggers analgetic drugs and opioid abuse, and increases overall treatment costs [2, 3]. Therefore, mental health conditions should always be assessed on patients after undergoing surgery. This review is aimed at giving insight about postoperative depression, screening and diagnosis of postoperative depression, and its treatment.

REVIEW

Postoperative Depression, Immunity, And Pain

Immunity of Patients with Postoperative Depression

Imflammatory response happens in the presence of psychological stress. Inflammatory responses via small messenger molecules production and proinflammatory cytokines like Interleukin (IL)-1b, IL-6, and Tumor Necrosis Factor (TNF) by macrophages. When depression occurs, the immune system is affected by a decrease in T-cell function [1].

Stress triggered by disease or intraoperative management will cause cortical increases, which affect serotonin. Lack of serotonin contributes to sleep disturbances, depressive mood, anorexia, and anxiety. Glucocorticoid stimulation also depends on the presence of proinflammatory cytokines, which are released in the presence of cell injury, which happens a lot during surgery [13].

Pain and Postoperative Depression

Pain is a multidimensional (sensory, emotional, and affective) experience. In the sen-

sory dimension, pain triggers perception of the stimulus location, quality, and intensity. In the emotional dimension, the body processes uncomfortable triggers from the stimulus. The affective dimension includes upset, sad, anxious, and depressed feelings as responses to the pain stimuli [1]. The intensity, duration and number of locations of pain is related to depression.

Chronic postoperative pain may occur if acute pain is not well-treated. In patients with chronic postoperative pain, depression often happens (30-100%). A study by Hinrichs-Rocker et al found that there is a strong correlation between depression and postoperative chronic pain. Pain and depression worsens each other [1, 14]. In the event of chronic pain, neuroinflammation happens, in which primary sensoric neuron's activities increase and cause peripheral neuron damage. Glial cells and mast cells are related to chronic pain. In chronic inflammation, microglia increase and give stronger responses to the next inflammation stimulation. Mast cells undergo degranulation, which activates the pain pathway, causes hypersensitivity to tactile pain, and causes the production of a substance that can increase the sensitivity of other nociceptros [15]. A study stated that thoracoscopic surgery, a less-invasive procedure compared to thoracotomy, is related to the decrease of postoperative depression and anxiety. Better lung function is also achieved [12]. Another study discovered that adequate management of pain decreases the incidence of postoperative depression. Subjects receiving high thoracic epidural analgesics (HTEA) have lower pain and cardiac depression scale (CDS) scores compared to those receiving intravenous morphine [16].

Postoperative Depression In Various Surgeries

Postoperative Depression in Coronary Artery Bypass Graft (CABG)

The prevalence of mental disturbances in post-CABG patients is about 30–40%. Post-CABG patients who suffer from depression have a higher incidence of morbidity and mortality. They are also at higher risk for arrythmia, recurrent angina, recovery problems, and problems in quality of life [1, 17]. nother study shows that levels of depression and anxiety are higher in patients after CABG procedures compared to before CABG. The mean score of Beck's Depression Inventory (BDI) before CABG is 8.12, and it increases to 12.43 after CABG. The mean score of Beck's Anxiety Inventory (BAI) before CABG is 11.28, and it increases to 18.26 after CABG [7].

Major depressive disorder or depression symptoms are related to cardiac symptoms. The more severe the depression symptoms, the worse the cardiac complications are. In coronary heart disease patients with depression, their cardiac markers showing atherosclerosis are higher compared to those without depression. In addition, an increase of C-reactive protein, IL-6, fibrinogen, thrombocyte activation, and vascular function damage are also present [18]. CABG is a major operation involving a vital organ. Patients may feel emotional and ehavioural changes caused by fear, anxiety, and uncertainty about the operation and the impact in their lives. The effects of depression and anxiety is sometimes worse than the cardiac complaints [7].

Postoperative Depression in Musculoskeletal Surgery

Patients suffering from low back pain typically caused by lumbar disc herniation experience chronic pain. Although procedures like lumbar discectomy have been done, the outcomes are not always good. Patients sometimes feel postoperative pain related to depression and recurrent surgeries. Depression prior to operation caused by chronic pain is also related to operation failure [1].

Postoperative depression is higher after a spine operation compared to other operations (CABG, hysterectomy, and cholecystectomy). A study by Wilson et al. stated that in patients with no prior depression, there is a 2.33 times increased risk of depression after undergoing the CABG procedure [8]. Spine

operation increased postoperative depression incidence by 5 times in patients without prior depression. Old age and female sex are risk factors for post-spinal operation depression [8]. Another study explained that the risk factors for post-spinal operation depression are old age, female sex, and low level of education [19]. In a study on patients with degenerative lumbar disease who underwent surgery, the prevalence of postoperative depression was 17.6% in 1 year [20].

In post-shoulder arthroplasty patients, a significant increase in depression scores happens in all patients (with or without prior depression). This proves the presence of postoperative depression in the shoulder arthroplasty procedure. The patients also have low satisfactions about the operation, although they experience less pain after the procedure [9].

Postoperative Depression in Cancer Surgery

Cancer is a terminal disease with a usually low survival rate. Patients with cancer have varying emotional and functional disturbances. A lot of cancer therapy, such as radiation, chemotherapy, and surgery, often causes distress and depression [10].

In breast cancer survivors who underwent mastectomy, the incidence of postoperative depression gets higher from year to year. The average of depression incidence before mastectomy is only 5%, while after 1 year of surgery it increases to 19%, and it increases even more 6 years after surgery to 23%, and finally reaches 67% in 10 years after surgery. Old age and comorbidities like ischaemic heart disease, cerebrovascular disease, and chronic obstructive pulmonary disease are independent risk factors for postoperative depression [10].

Esophageal and gastric cancer have severe adverse effects after surgery, including severe pain, dyspnea, food reflux, dysphagia, and diet restriction. Surgery is the only recommended curative treatment, although it is known to cause distress and postoperative quality of life tend to be low [11].

Pulmonary cancer patients who need pulmonary resection also experience an increase in postoperative depression and anxiety incidence. Before surgery, anxiety incidence is 8%, and it increases to 9% after surgery, while depression incidence increases from 12% before surgery to 19% after surgery. Thoracotomy is also a risk factor for postoperative depression and anxiety. Postoperative symptoms of dyspnea, severe pain, and diabetes mellitus comorbidity are also risk factors for postoperative depression [12].

Impact Of Postoperative Depression

Impact on Patient Disability and Quality of Life

Major depression is often associated with a decrease in daily function and quality of life. This also applies to patients with postoperative depression [1]. In a study by Dragomir et al., patients undergoing surgeries for breast cancer were assessed with BDI and State Trait Anxiety Inventory 1 (STAI-X1), then assessed for quality of life with the Quality-of-Life Questionnaire. 7 days after surgery. The result is a decrease in quality-of-life score in patients with postoperative depression and anxiety. There were also significant correlations between postoperative depression and anxiety with fatigue, pain, insomnia, constipation, and appetite loss. Functional disability is also increased in patients with postoperative depression and anxiety [21].

A study by Trezivan et al. also concludes that depression is associated with somatic and behavioral changes. Somatic changes that occur are energy decrease, sleep pattern and appetite changes, difficulty concentrating, tiredness, and fatigue. In patients who underwent heart transplantation, 91% had minimal depression, 6% had mild depression, and 3% experienced moderate depression. Their quality of life (physical, psychological, social, and environmental domains) were assessed using the World Health Organization Quality of Life-BREF (WHOQOL-BREF), and the result is that women have lower scores compared to men (61,63 vs. 71,01) [22]. Sleep disturbance in pa-

tients with depression was also reported by Angkawidjaja and Soetjipto [23]. Dujmovic et al. explain that there is a significant correlation between the decrease in depression severity and the increase in quality of life. Depression also significantly correlates with patients' degree of pain [24].

Impact on Mortality

A community meta-analysis study found depression increases mortality risk. Another study stated that post-bariatric surgery patients have a higher suicide rate. Tindle et al. stated that the suicide rate of post-bariatric surgery male patients is 13.7 in 10.000 and in female patients, it is 5.2 in 10.000, while the suicide rate in the general population is only 0.7-2.4 in 10.000 [25].

In post-CABG patients with postoperative depression, 1-year mortality is increased in comparison to patients with no depression symptoms. The mortality risk is 1.05 times higher in male and 1.07 in female patients. Depression occurring before CABG is also associated with a mortality rate increase, in which the risk is 1.05 times higher [17].

Differential Diagnosis of Postoperative Depression

Postoperative psychiatric disorders are a spectrum of psychiatric diseases in postoperative patients. According to DSM-5, the diagnosis of postoperative psychiatric disorders is made in patients with no diagnosis of psychiatric disorder before surgery [26] Among the postoperative psychiatric disorders are listed below [27].

Brief Psychotic Disorder

By definition, a brief psychotic disorder is acute-onset psychosis, which happens for less than 1 month with complete remission. Psychotic symptoms experienced may include delusions, hallucinations, incoherent speech, and catatonic or inorganized behavior. It often occurs along with real stressors and is called brief reactive psychosis [28, 29]. In a study involving 100 patients undergoing thorax surgery, among the 18 patients who suffer from postoperative psychiatric disorders, 6% suffered from psychosis [27].

Delirium

Delirium is a syndrome involving acute changes in consciousness, fluctuative consciousness, or attention, behavioral, and memory disorders [28]. In a study by Ozyurtkan et al., delirium is the largest cause of postoperative psychiatric disorders (44%). It is hypothesized that delirium is related to the central nervous system response to systemic inflammation and chemokine increase, which enables blood-brain barrier damage [27].

Acute Stress Disorder and Adjustment Disorder

Reaction to stress and adjustment disorder are among the differential diagnoses of postoperative depression. But Post-Traumatic Stress Disorder (PTSD) can be diagnosed if it occurs in 6 months, along with recurrent traumatic flashbacks and autonomic diruptions [28]. Adjustment disorder contributes in 22% of the postoperative psychiatric disorder cases [27].

Panic Attack

Panic attack is caused by an increase in sympathetic tone related to hormon release via hypothalamic-pituitary-adrenal system, which causes stress response or fight-or-flight response. Panic attacks play a role in 22% of the postoperative psychiatric disorder cases [27].

Management of Postoperative Depression

Park et al recommend that patients with Hospital Anxiety Depression Scale (HADS) score >11 need postoperative psychiatric management [12].

D	A		D	A	
		I feel tense or 'wound up':			**I feel as if I am slowed down:**
	3	Most of the time	3		Nearly all the time
	2	A lot of the time	2		Very often
	1	From time to time, occasionally	1		Sometimes
	0	Not at all	0		Not at all
		I still enjoy the things I used to enjoy:			**I get a sort of frightened feeling like 'butterflies' in the stomach:**
0		Definitely as much		0	Not at all
1		Not quite so much		1	Occasionally
2		Only a little		2	Quite Often
3		Hardly at all		3	Very Often
		I get a sort of frightened feeling as if something awful is about to happen:			**I have lost interest in my appearance:**
	3	Very definitely and quite badly	3		Definitely
	2	Yes, but not too badly	2		I don't take as much care as I should
	1	A little, but it doesn't worry me	1		I may not take quite as much care
	0	Not at all	0		I take just as much care as ever
		I can laugh and see the funny side of things:			**I feel restless as I have to be on the move:**
0		As much as I always could		3	Very much indeed
1		Not quite so much now		2	Quite a lot
2		Definitely not so much now		1	Not very much
3		Not at all		0	Not at all
		Worrying thoughts go through my mind:			**I look forward with enjoyment to things:**
	3	A great deal of the time	0		As much as I ever did
	2	A lot of the time	1		Rather less than I used to
	1	From time to time, but not too often	2		Definitely less than I used to
	0	Only occasionally	3		Hardly at all
		I feel cheerful:			**I get sudden feelings of panic:**
3		Not at all		3	Very often indeed
2		Not often		2	Quite often
1		Sometimes		1	Not very often
0		Most of the time		0	Not at all
		I can sit at ease and feel relaxed:			**I can enjoy a good book or radio or TV program:**
	0	Definitely	0		Often
	1	Usually	1		Sometimes
	2	Not Often	2		Not often
	3	Not at all	3		Very seldom

Picture 1. Hospital Anxiety Depression Scale (HADS) [12]

In the therapy of depression there are some modality choices, which are psychopharmacology and psychotherapy [30, 31]. In postoperative depression, besides the regular therapy for depression, adequate pain management should always be kept in mind [32].

Psychopharmacology

Psychopharmacology given to depressed patients is antidepressant. The aim of psychopharmacology is to achieve complete remission of all depression symptoms and signs, improve patient psychosocial and work functions, and prevent relaps or recurrent depression. A lot of antidepressants have good efficacy. In giving therapy, some considerations like patient factors, general medical condition, tolerability and adverse effects, and drug availability should be kept in mind. Based on those factors, there is a recommendation for choosing antidepressant therapy [30].

Tricyclic and tetracyclic antidepressants work by non-selectively inhibiting the uptake of neurotransmitters released from pre-synaptic neurons to synaptic clefts. Because of their non-selective nature, a lot of adverse effects may happen. Serotonin selective reuptake inhibitors (SSRI) work similarly, but their inhibition is selective to serotonin (5HT2). Reversible inhibitor of MAO-A (RIMA) works in pre-synaptic neurons, inhibiting the monoaminase enzyme that breaks and metabolizes serotonin. SNRI works by inhibiting serotonin and norepinephrine reuptake, so its concentration increases in post-synaptic neurons [30]. Tricyclic antidepressants and serotonin-norepinephrine reuptake inhibitors (SNRI) are also beneficial in the management of postoperative chronic pain, which is an essential factor to consider for postoperative patients' treatment [32].

According to a meta-analysis by Magni et al., sertraline has higher efficacy than fluoxetine. Both are SSRI [33]. This drug group is also

quite safe for patients with hypertension, although routine monitoring of blood pressure is needed [34]. ntidepressant therapy needs a long time, which may take years to complete. The long duration is aimed to achieve remission and prevent relapse. Antianxiety medicine, consisting of benzodiazepines, is quite commonly added to the therapy of depression. They are temporary and not given in the long run. Antianxiety is usually added if the patient experiences symptoms of anxiety [35, 36].

Treatment choice should also consider drug interactions with the patient's main disease. Tricyclic antidepressants (TCA) may cause heart dysrhythmia. Epinephrine and norepinephrine prolong TCA's duration of action and increase its effects. The use of RIMA and ephedrine may cause hypertension crises. Simultaneous usage of SSRI or SNRI with meperidine or tramadol increases the risk of serotonin syndrome. SSRI is also associated with an increased risk of spontaneous hemorrhage caused by intraplatelet serotonin decrease [37].

Psychotherapy

The aim of psychotherapy is to develop patientsmechanisms of defense in facing stressors. The kind of psychotherapy given to the patient depends on the patient's needs, such as supportive, reeducative, and reconstructive Supportive psychotherapy helps broaden the patient's controlling mechanism to be more adaptive. Reeducative psychotherapy changes patients's mindsets by forming beneficial routines and abandoning bad life routines, like behavioral therapy. Reconstructive psychotherapy changes the patient's thought structure [38].

A study by Qiu et al. found that cognitive behavioral therapy (CBT) has a good effect on the recovery of patients after undergoing mastectomy. Using the Hamilton Depression Rating Scale assessment, the score of the CBT group is significantly lower than the control group in 6 months. Quality of life and self-confidence are also better in the CBT group [39].

In a study on post-cancer operation patients, emotional competence and emotional intelligence have good impacts on patients. Emotional competence includes emotional identification, understanding, and regulation [11]. Ghoneim and O'Hara found that early detection and treatment for depression prior to surgery is beneficial in decreasing the diseases' adverse effects, surgery failure, and postoperative depression. Monitoring of mental condition and after surgery are also associated with a decrease in morbidity and mortality of postoperative patients [1].

CONCLUSION

Postoperative depression often happens with no prior depression symptoms and in successful operations. Its incidence is related to the change in neurotransmitters caused by intraoperative management that triggers physical stress. Postoperative depression affects patients' immune systems by increasing inflammatory responses caused by psychologic stress. Postoperative depression is also affected by acute pain, which is often not adequately treated after surgery. Postoperative chronic pain may happen because of this, and it further worsens patients' mental health and increases the incidence of depression.

A lot of studies explaining depression after a variety of surgeries (CABG, musculoskeletal operation, cancer operation, etc.) show increased incidence of depression. Postoperative depression is related to an increase in pain after the surgery, postoperative complications, recurrent symptoms, prolonged length of stay, and a decrease in quality of life. Another important thing is that mortality is also increased in patients with postoperative depression.

Screening for postoperative depression can be done using the Hospital Anxiety Depression Scale. Psychopharmacology and psychotherapy are the treatments for postoperative depression. Adequate management of pain should also be considered. In choosing the psychopharmacology for postoperative

treatment, besides the drug's efficacy, physicians should also consider its capacity for pain management and its interaction with other drugs.

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CONFLICT OF INTEREST

The author declares that there is no conflict of interest

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