SYSTEMATIC REVIEW

Factors related to loss of appetite in postoperative cardiac surgery patients: A systematic review [version 1; peer review: 1 approved with reservations]

Channarong Prasankok¹, Samoraphop Banharak²

¹Nursing Department, Queen Sirikit Heart Center of the Northeast, Khon Kaen University, Khon Kaen, Thailand, 40002, Thailand

²Gerontological Nursing Department, Faculty of Nursing, Khon Kaen University, Khon Kaen, Thailand, 40002, Thailand

V1 First published: 06 May 2021, 10:350
<https://doi.org/10.12688/f1000research.52287.1>

Latest published: 06 May 2021, 10:350
<https://doi.org/10.12688/f1000research.52287.1>

Abstract

Background: Postoperative cardiac surgery patients often experience appetite loss. Although nutritional status is known to be associated with time of recovery, functional status, and length of stay, less is known about factors related to patient's loss of appetite after cardiac surgery. This review aimed to identify and understand factors related to loss of appetite in postoperative cardiac surgery patients, systematic review with narrative summary design was applied. Data sources including CINAHL, SCOPUS, PubMed, ProQuest, ScienceDirect, ThaiLIS, ThaiJo, and E-Thesis were searched without restriction on publication year through August 2020.

Methods: We conducted the review following the Joanna Briggs Institute methodology, using the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) checklist to categorize methodological quality and the PRISMA flow diagram to record the studies' factors.

Results: Six studies reported one or more of 16 factors related to loss of appetite: older age, sex (female), illiteracy, history of chronic disease, not knowing someone in health field, pain score ≥ 7 , pain medications containing codeine, constipation, depression, heart-lung machine ≥ 120 minutes, preoperative serum creatinine levels ≥ 179 $\mu\text{mol/L}$, emergency surgery, perfusion pressure ≤ 40 mmHg, low cardiac output syndrome, mechanical ventilation ≥ 96 hours, and a New York Heart Association class III and IV.

Conclusion: The small number of publications restrict our conclusions. Future research should focus on multiple factors related to appetite loss in postoperative cardiac surgery patients. Additional research will provide a foundation for evidence-based interventions to reduce appetite loss and improve patient nutritional status after cardiac surgery. Nurses and other health professionals should assess postoperative cardiac surgery patients for the presence of the 16 significant factors. To promote patients' nutritional status, there

Open Peer Review

Approval Status ?

1

version 1

06 May 2021

?

[view](#)

1. **Bingyang Ji** , Chinese Academy of Medical Sciences, Beijing, China

Any reports and responses or comments on the article can be found at the end of the article.

should be evidence-based practice guidelines on the management of postoperative symptoms such as pain management, treatment of constipation, and reduction of emotional stress and depression.

Keywords

anorexia, cardiac surgery, heart surgery, loss of appetite, poor appetite, systematic review

Corresponding author: Samoraphop Banharak (sbanharak@kku.ac.th)

Author roles: **Prasankok C:** Conceptualization, Data Curation, Formal Analysis, Investigation, Methodology, Project Administration, Resources, Software, Validation, Visualization, Writing – Original Draft Preparation, Writing – Review & Editing; **Banharak S:** Conceptualization, Data Curation, Formal Analysis, Funding Acquisition, Investigation, Methodology, Project Administration, Resources, Software, Supervision, Validation, Visualization, Writing – Original Draft Preparation, Writing – Review & Editing

Competing interests: No competing interests were disclosed.

Grant information: This work was financially supported by the Research and Training Center of Enhancing Quality of Life of Working Age People, Faculty of Nursing, Khon Kaen University (Grant Number RGS64-003) and Research and Graduate Studies, Khon Kaen University (Grant Number FM64-003). Appreciation is extended to these research and training centers for making our research possible. *The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.*

Copyright: © 2021 Prasankok C and Banharak S. This is an open access article distributed under the terms of the [Creative Commons Attribution License](#), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

How to cite this article: Prasankok C and Banharak S. **Factors related to loss of appetite in postoperative cardiac surgery patients: A systematic review [version 1; peer review: 1 approved with reservations]** F1000Research 2021, 10:350 <https://doi.org/10.12688/f1000research.52287.1>

First published: 06 May 2021, 10:350 <https://doi.org/10.12688/f1000research.52287.1>

Introduction

Heart disease is one of the leading causes of death in both developed and developing countries¹. Although treatment depends on severity and types of heart disease, first line approaches include lifestyle changes involving nutrition, exercise, and medication. As patients' symptoms worsen or complications increase, cardiac surgery often becomes the next treatment of choice¹.

There are various types of cardiac surgery. These include coronary artery bypass graft, valve replacement and repair, great vessel surgery, and septum repair for those with congenital heart disease. Most of these surgeries require the use of the heart-lung machine as a cardiopulmonary bypass to take over the function of the heart and lungs during surgery to help surgeons repair a diseased heart's malfunctioning. Because there have been adverse effects from using the heart-lung machine on the various body systems, an off-pump coronary artery bypass technique was developed as an alternative². Nevertheless, the cardiopulmonary bypass remains widely used during open heart surgery. Prevention and management of possible deleterious effects from its use require ongoing assessment.

Background

Alterations in postoperative physiological/psychological functioning contribute to loss of appetite. Surgery and the use of the heart-lung machine cause injuries in tissues and peripheral nerves that can lead to a nociceptive and inflammatory response, causing prostaglandins, bradykinins, and substance P to become increased that produces physical pain³. Postoperative pain and the use of the heart-lung machine are stressors that produce a physiological response such as the systemic inflammatory response syndrome³. The syndrome is a disturbance in the balance of the coagulation system that decreases the production of platelets and fibrinogen with increases in prothrombin time, leading to a higher risk of postoperative bleeding⁴. The immune system responds by decreasing the polymorphonuclear neutrophils and also macrophages in the lungs, which heighten the risk of infections, including pneumonia⁵. Cardiac surgery also intensifies catabolism and insulin resistance, resulting in higher blood sugar levels in both patients with and without a history of diabetes⁶. These factors directly and indirectly disturb the postoperative physiological/psychological interconnections to produce a loss of appetite and a nutritional imbalance⁷.

Food consumption behaviors change when patients consume small volumes of food, coupled with physical decline, less body movement/mobility, depression, and postoperative stress. Ścisło *et al.* (2019) found that after the cardiac surgery, 50% of patients had loss of appetite with an increased risk of poor nutrition, 35.4% had postoperative complications, and 10% had a decreased body mass index (BMI)⁸. The study affirmed that a decrease in BMI after surgery is associated with postoperative complications⁹. Chermesh *et al.* (2014) found similarly that poor nutritional status increases the severity and number of complications in postoperative patients¹⁰. Ringaitienė *et al.* (2016) reported that recovery is delayed in patients who have a loss of appetite and consume less food, causing longer hospitalizations¹¹.

Based on clinical experiences in caring for patients who had undergone cardiac surgery, we observed that some patients had decreased appetite, difficulty eating, ate less or had early satiety, and suffered bouts of nausea and vomiting. We further observed that these same postoperative cardiac surgical patients tended to have a late recovery, longer duration of hospitalization, and poorer prognosis than others without the symptoms. To the best of our knowledge, we found no literature that summarized and explained our observations. Therefore, the purpose of this systematic review of the literature was to contribute to a body of knowledge by focusing on all known factors related to loss of appetite in postoperative cardiac surgery patients. Understanding these factors will provide a foundation that is necessary to support nursing practice of cardiac surgical patients and inform future researchers what further aspects of loss of appetite need to be studied.

Purpose

The purpose of this review was to systematically identify and understand the collective factors related to loss of appetite in postoperative cardiac surgery patients as found in published research.

Methods

Design

We followed the systematic review process with narrative summary as prescribed by the Joanna Briggs Institute (JBI) methodology by formulating the review question, defining the inclusion and exclusion criteria, developing the search strategy, locating and selecting studies, assessing their quality, extracting data, and analyzing and interpreting the results¹². Moreover, the protocol for systematic review was registered at PROSPERO on February 1, 2021 and registration number was CRD42021234615.

Search methods

We searched CINAHL, SCOPUS, PubMed, ProQuest, ScienceDirect, ThaiLIS, ThaiJo, and E-Thesis databases and used snowballing through reference lists of defined studies. The search for both English and Thai published papers was made without restriction on publication year through August 2020. The search strategy used the keywords “cardiac surgery” OR “open-heart surgery” AND “poor appetite” OR “loss of appetite” OR “decreased appetite” OR “change in appetite” OR “anorexia.” The selection of studies was made based on the following inclusion criteria: (a) research in humans related to cardiac surgery; (b) results about factors related to loss of appetite in postoperative cardiac surgery patients; (c) patients aged 18 years and older; and (d) published in the English or Thai language.

Search outcomes

There were 5,774 original studies from the databases and two from hand searches. The winnowing process began with deduplication, which left 3,320 studies. Only 74 studies had full-text availability, of which 68 were excluded because they did not fully meet the inclusion criteria. As a result, six empirical research articles remained for appraisal. **Figure 1** displays the PRISMA flow diagram of the information flow during the review process.

Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) Flowchart of the Review Process.

Quality appraisal

We individually reviewed the six selected articles using the standardized critical appraisal instrument from the JBI for analytical cross-sectional studies¹³. The studies were required to meet a positive response (i.e., “yes”) on a minimum of four of the eight questions on the critical appraisal tool. Methodological quality was grouped into the four categories of very low, low, moderate, and high quality.

Data abstraction

On the JBI data extraction form (Aromataris & Munn, 2018)¹², we recorded the studies’ authors, study designs, settings, participants, levels of evidence certainty and methodological quality, types of surgery, times of outcomes measuring, and

factors related to loss of appetite. Prior to starting the review, we practiced article screening, data extraction, and quality assessment with two other researchers who independently verified that the process and results we had undertaken were accurate. If there were incongruent opinions during the actual review process, we reached consensus in mutual discussion.

Synthesis

Extraction of quantitative data to conduct meta-analysis was not possible due to the heterogeneity of the study population, different types of cardiac surgery, outcome measures, and data analysis across the studies. The findings have been presented and discussed in tabular and narrative form to aid the data presentation.

Results

Six research articles met the inclusion criteria^{14–19}. They were all descriptive studies. Five had a moderate level of quality, and one had a high level of quality (Table 1 & Table 2). Two studies were published before the year 2000^{16,17}, and four were published on or after 2000^{14,15,18,19}. Patients in five studies had undergone coronary artery bypass graft surgery^{14,16–19}; patients in three studies had undergone valve surgery^{15,16,19}; and patients in one study had both a septum repair for congenital heart disease and a repair of the aorta¹⁹. The surgeries reported in five studies required cardiopulmonary bypass^{14–16,18,19}, whereas one study did not specify its use¹⁷. Although five studies addressed patients postoperatively and after-discharge^{14–18}, one study described the preoperative, operative, and postoperative phases¹⁹ (Table 3).

There were 16 factors identified in the six studies related to loss of appetite and they were divided into three phases. *The preoperative factors* were (a) age ≥ 60 years old; (b) sex (female); (c) history of a chronic disease, such as diabetes, hypertension, hyperlipidemia; (d) illiteracy; (e) not knowing someone in the health field; and (f) preoperative serum creatinine level $\geq 179 \mu\text{mol/L}$. *The operative factors* were (a) emergency surgery; (b) using the heart-lung machine ≥ 120 minutes; (c) perfusion pressure ≤ 40 mmHg; and (d) low cardiac output syndrome. Finally, *the postoperative factors* were (a) using mechanical ventilation ≥ 96 hours; (b) moderate or higher pain score (≥ 7 points); (c) using pain medications containing codeine; (d) constipation; (e) depression; and (f) New York Heart Association (NYHA) class III and IV. Nevertheless, the study of Zang *et al.* (2009)¹⁹ reported specifically that the patient's sex and types of cardioplegia solutions had no impact on loss of appetite in postoperative cardiac surgery patients (Table 3).

Discussion

We found that there were 16 factors related to loss of appetite in cardiac surgery patients. They were present in the preoperative, operative, or postoperative/discharge phases.

Preoperative phase

The aging process in itself can produce a loss of appetite due to a decrease in taste and smell, resulting in discontent with eating and a poor appetite²⁰. Older people (≥ 60 years) experience a decrease in ghrelin or a hunger hormone, an increase in leptin and insulin, and changes in the gastrointestinal system and inflammatory process, such as an increase in interleukin 1 (IL-1) and 6 (IL-6) and tumor necrosis factor alpha (TNF- α)²¹ that contribute to a loss of appetite. Older females, with low estrogen levels transitioning through menopause or post menopause can also have a loss of appetite²⁰. Whether males or females are more likely to have a loss of appetite with cardiac surgery, however, needs further study, since Zang *et al.* (2009) found there was no statistical difference between the two¹⁹. Chronic disease, such as diabetes or hypertension, can lead to an inflammatory process and an increase in interleukin and tumor necrosis factor alpha, which are known to be related to appetite^{22,23}. Moreover, increased blood sugar and high blood pressure can produce physiological stress. Both may directly and indirectly

cause loss of appetite by pathophysiological and psychological pathways⁷.

Illiterate patients and those who do not know someone in the health field tend to experience loss of appetite. They may be less knowledgeable and unsure of self-care activities or uncomfortable and inexperienced in seeking help with their health and nutrition problems. Cebeci and Celik (2008) and Choocherd *et al.* (2016) also found that low health literacy was related to nutritional problems in coronary artery bypass graft surgery patients^{24,25}. High preoperative serum creatinine also affects loss of appetite, but indirectly^{24,25}. A decline in glomerular filtration is associated with reduced food intake^{26–28}. Although hospitals are not traditionally known for tasty cuisine, prolonged lengths of stay in an intensive care unit can produce depression that may lead to a lack of appetite^{26,29,30}.

Operative phase

During the use of the heart-lung machine, chemical substances are produced by a systemic inflammatory response named proinflammatory cytokine³¹. This substance includes interleukin (IL), tumor necrosis factor alpha (TNF- α), interferon gamma (IFN γ) and granulocyte-macrophage colony stimulating factor (GM-CSF). Higher levels of chemical substances are strongly related to loss of appetite. These chemical substances also become substantially increased in patients with cancer, affecting appetite. After the heart-lung machine is disconnected, the substances can remain at high levels for 48 hours after surgery³². Not only does the heart-lung machine produce a systemic inflammatory response, but the digestive system is interrupted. Prolonged use of the heart-lung machine can lead to weariness and loss of appetite after cardiac surgery³².

Low cardiac output syndrome, low perfusion pressure, and emergency surgery may indirectly affect loss of appetite. These three factors correlate with extended stays in the intensive care unit, total lengths of hospitalization, and prolonged intubation times^{26,28}. Low cardiac output and low perfusion pressure place patients at risk of acute kidney injury that can lead to high serum creatinine; and emergency cardiac surgery causes more postoperative complications in patients than planned surgery^{26,27,33}. These three conditions may collectively bring about stress and depression, leading to loss of appetite^{26,29,30,34}.

Postoperative phase

Prolonged mechanical ventilation requires suctioning patients' endotracheal tubes to clear the airway, leading to post-extubation fatigue and loss of appetite. It is a significant factor affecting patients' appetite levels after their endotracheal tubes are removed. Longer periods of postoperative mechanical ventilation are also influenced by higher levels of preoperative creatinine, low cardiac output, and psychological depression, further contributing to loss of appetite³⁵. Depression itself is a source of appetite loss by the hypoactivation of the brain's insular regions, especially mid-insular cortex that supports the body's physiological control of eating³⁶. Depressed patients have an increase in their hypothalamic-pituitary-adrenal drive that can cause high levels of cortisol, which is

Table 1. The results of critical appraisal for the selected six analytical cross-sectional studies.

Critical Appraisal Checklist for Analytical Cross-sectional Studies (Joanna Briggs Institute) ¹³										
Studies	Were the criteria for inclusion in the sample clearly defined?	Were the study subjects and the setting described in detail?	Was the exposure measured in a valid and reliable way?	Were objective, standard criteria used for measurement of the condition?	Were confounding factors identified?	Were strategies to deal with confounding factors stated?	Were the outcomes measured in a valid and reliable way?	Was appropriate statistical analysis used?	scoring	Overall appraisal (include)
Grap <i>et al.</i> , 1996 ¹⁶	✓	✓	✓	✓	-	-	✓	✓	6/8	✓
King & Parrinello, 1988 ¹⁷	✓	✓	✓	✓	-	-	✓	✓	6/8	✓
Corrêa & Cruz, 2000 ¹⁵	✓	✓	✓	✓	✓	✓	✓	✓	8/8	✓
Miller & Grindel, 2004 ¹⁸	✓	✓	✓	✓	-	-	✓	✓	6/8	✓
Zhang <i>et al.</i> , 2009 ¹⁹	✓	✓	✓	✓	-	-	✓	✓	6/8	✓
Ammouri <i>et al.</i> , 2016 ¹⁴	✓	✓	✓	✓	-	-	✓	✓	6/8	✓

associated with decreased appetite and hypoactivation of food-motivation neurocircuitry^{30,34,37}. The interactivity and interaction among these regions, however, contribute to individual differences in patients with depression-related appetite changes³⁶.

After open heart surgery, patients experience pain and discomfort during routine postoperative care, such as deep breathing and coughing to expand the lungs and clear secretions, using an incentive spirometer, moving/turning in bed coupled with early ambulation, and undergoing physical therapy with possible rehabilitation activities. Pain decreases the movement and mobility of patients, so the stomach and intestine are relatively less functional³⁸. Patients can feel anxious, insecure, and uncertain about the disease and success of the surgery, causing them to have emotional stress. These complicated reactions are intercorrelated and can affect the appetite directly and indirectly. As a result, these patients may experience a decrease in appetite with a distorted perception of smell and gustatory dysfunction, leading to a lower consumption of food³⁹.

Pain that occurs immediately after cardiac surgery is called acute pain, whereas pain after hospital discharge is chronic pain. Both can stimulate the inflammatory process, which causes the release of cytokine, especially IL-6^{40,41}. Interleukine-6 is related to loss of appetite. Because the release of cytokine leads to the pain cycle, postoperative patients require analgesics, usually with codeine^{42,43}. Medications containing codeine

coupled with less physical movement and stomach/intestinal dysfunction may cause constipation. Constipation affects loss of appetite because patients feel that food remains in the gastrointestinal system, which produces abdominal discomfort^{38,44}.

Patients with NYHA Class III & IV heart failure may have a loss of appetite due to hypervolemia, especially if there is congestion in the lungs, liver, and intestine⁴⁵. Congestion directly affects the function of the respiratory and gastrointestinal systems, producing dyspnea, fatigue, and inactivity, all related to loss of appetite. Liver and intestinal congestion leads to gastrointestinal hypomotility of the stomach and intestine⁴⁶. This may cause abdominal distension and discomfort, thus inhibiting patient activities would stimulate appetite. In addition, medications that treat and control heart failure, such as digoxin and simvastatin, not only impact appetite indirectly by affecting the function of the gastrointestinal system but also decrease appetite directly^{46,47}.

Five out of the six studies had a moderate level of methodological quality^{14,16–19}. The researchers did not report their confounding factors, missing data, or how they managed the statistical challenges. Only one study (Corrêa & Cruz, 2000) reported controlling for two confounding factors that may have affected loss of appetite (i.e. level of pain and onset of having pain)¹⁵. Pain is both a rapidly (state variable) and slowly (trait variable) changing factor^{48,49}. A state variable can change in a short time period and at a specific moment, whereas a trait variable takes much longer to change. Corrêa and Cruz (2000) divided

Table 2. Grading results of the six selected studies from the quality assessment of the evidence by GRADE guideline¹³.

Quality Assessment of the Evidence by GRADE Guideline									
No.	^a Risk of bias (confounding factors, missing data, adherence measurement)			^b Precision (statistical certainty, amount of information on a certain factor how precisely an object of study is measured)			^c Directness (extent to which the people, interventions, and outcome measures are similar to those of interest, confident results come from the direct evidence)		Certainty of evidence
	Low	Unclear	High	Precise	Imprecise		Direct	Indirect	
Grap <i>et al.</i> , 1996 ¹⁶		✓		✓			✓		Moderate
King & Parrinello, 1988 ¹⁷		✓		✓			✓		Moderate
Corrêa & Cruz, 2000 ⁵			✓	✓			✓		High
Miller & Grindel, 2004 ¹⁸		✓		✓			✓		Moderate
Zhang <i>et al.</i> , 2009 ¹⁹		✓		✓			✓		Moderate
Ammouri <i>et al.</i> , 2016 ¹⁴		✓		✓			✓		Moderate

^a = Risk of bias; ^b = Precision; ^c = Directness; ^d = Consistency

GRADE Working Group Grades of Evidence for certainty of evidence

High: The research provides a very good indication of the likely effect. The likelihood that the effect will be substantially different is low.

Moderate: The research provides a good indication of the likely effect. The likelihood that the effect will be substantially different is moderate.

Low: The research provides some indication of the likely effect. The likelihood that it will be substantially different (a large enough difference that it might have an effect on a decision) is high.

Very low: The research does not provide a reliable indication of the likely effect. The likelihood that the effect will be substantially different (a large enough difference that it might have an effect on a decision) is very high.

Table 3. A summary of the reviewed studies and factors related to poor appetite in postoperative cardiac surgery patients.

Authors	Study Design	Setting	Participants	Level, Certainty of Evidence and Methodological Quality ^a	Types of Surgery	Time of Outcomes Measured	Factors Related to Loss of Appetite
Grap <i>et al.</i> , 1996 ¹⁶	Observational analytical study without a control group	A large university medical center	34	Level 3.e ⊕⊕⊕○ Moderate ^a (6/8)	Coronary artery bypass graft surgery/None	After discharge	<ul style="list-style-type: none"> - Constipation - A pain medication containing codeine
King & Parrinello, 1988 ¹⁷	Observational analytical study without a control group	Two medical school hospitals	122	Level 3.e ⊕⊕⊕○ Moderate ^a (6/8)	Coronary artery bypass graft surgery and valve surgery/ Cardio-pulmonary bypass surgery	After discharge	<ul style="list-style-type: none"> - Depression was correlated with poor appetite at 2nd and 6th weeks after discharge.
Corrêa & Cruz, 2000 ¹⁵	Observational analytical study: cohort study	Not available	80	Level 3.c ⊕⊕⊕⊕ High (8/8)	Heart Surgery/Cardio-pulmonary bypass surgery	Postoperative	<ul style="list-style-type: none"> - Pain score ≥ 7 was related to loss of appetite after surgery
Miller & Grindel, 2004 ¹⁸	Observational analytical study without a control group	University hospital	102	Level 3.e ⊕⊕⊕○ Moderate ^a (6/8)	Coronary artery bypass graft surgery/Cardio-pulmonary bypass surgery	Postoperative	<ul style="list-style-type: none"> - Age ≥ 65 years was related to loss of appetite at 6th week after surgery
Zhang <i>et al.</i> , 2009 ¹⁹	Observational analytical study: Case-controlled study	Hospital	412 (206 for study group and 206 for control group)	Level 3.d ⊕⊕⊕○ Moderate ^a (6/8)	Coronary artery bypass graft surgery, repair of congenital heart disease, valve replacement, aortic operation/Cardio-pulmonary bypass surgery	Pre/Under/ Postoperative	<ul style="list-style-type: none"> - Sex (non-significant) - Cardioplegia: Cold crystal, warm blood, cold blood (non-significant) - Cardiopulmonary bypass time > 120 minutes - Preoperative serum creatinine ≥ 179 $\mu\text{mol/L}$ - Emergency surgery - Perfusion Pressure $\leq 40\text{mmHg}$ - Low cardiac output syndrome - On ventilator ≥ 96 hours - Age ≥ 61 years - Heart failure NYHA Class III & IV
Ammouri <i>et al.</i> , 2016 ¹⁴	Observational analytical study without a control group	Two teaching hospitals and three private hospitals	100	Level 3.e ⊕⊕⊕○ Moderate ^a (6/8)	Coronary artery bypass graft surgery/Cardio-pulmonary bypass surgery	Postoperative	<ul style="list-style-type: none"> - Age ≥ 60 years - Female - Illiteracy - Chronic disease (e.g. diabetes, hypertension, dyslipidemia) - Not knowing somebody in health field

Authors	Study Design	Setting	Participants	Level, Certainty of Evidence and Methodological Quality [†]	Types of Surgery	Time of Outcomes Measured	Factors Related to Loss of Appetite
Joanna Briggs Institute levels of evidence Level 3.c - Observational analytical study: Cohort study with control group Level 3.d - Observational analytical study: Case-controlled study Level 3.e - Observational analytical study: Observational study without a control group							
GRADE Working Group Grades of Evidence for certainty of evidence High: The research provides a very good indication of the likely effect. The likelihood that the effect will be substantially different is low. Moderate: The research provides a good indication of the likely effect. The likelihood that the effect will be substantially different is moderate. Low: The research provides some indication of the likely effect. The likelihood that it will be substantially different (a large enough difference that it might have an effect on a decision) is high. Very low: The research does not provide a reliable indication of the likely effect. The likelihood that the effect will be substantially different (a large enough difference that it might have an effect on a decision) is very high.							
Explanations a. Risk of bias (low, unclear, high) b. Consistency (consistency, inconsistency, unknown/non applicable) c. Directness (direct, indirect) d. Precision (precise, imprecise)							

[†]The scores of Methodological Quality of the Studies are shown in fractions based on Joanna Briggs Institute and the Mixed Methods Appraisal Tools.
 ⊕○○○ = Very low quality; ⊕○○○ = Low quality; ⊕⊕○○ = Moderate quality; ⊕⊕⊕○ = High quality

the samples into several groups based on the level and onset of pain and compared the differences of loss of appetite between each group to identify more clearly the factors related to loss of appetite¹⁵. Because only one of the six studies demonstrated high methodological quality by controlling for confounding factors, we cannot make firm conclusions on the overall results of the systematic review¹².

Some of the 16 factors we report are not exclusive to postoperative cardiac surgery patients. Other types of surgery can produce changes in eating behaviors, food intake, loss of appetite, and malnutrition in postoperative patients. Factors may include older age^{50,51}; sex (female)^{50–52}; type of illness or chronic disease, such as type 2 diabetes mellitus^{50,52}; medications⁵⁰; length of hospital stay⁵⁰; and psychological factors, such as stress, depression, psychopathology, and well-being⁵³. In addition to those reported for general surgery patients, our systematic review expanded knowledge of other specific factors related to loss of appetite in postoperative cardiac surgery patients.

Strengths and limitations

We searched extensively the published literature in eight national and international databases, restricting the studies to those in English or Thai. Out of a large potential number of studies, only six met the specific criterion related to loss of appetite in postoperative cardiac surgery patients^{14–19}. None of the studies had loss of appetite as a primary research objective. Methodological problems in some studies could have been strengthened by having larger sample sizes, reporting how missing data were handled, and mentioning how confounding factors were controlled^{14,16–19}. In the studies with a larger sample size, subgroup analysis on individual factors could have brought better understanding of their influence on loss of appetite¹⁹. None of the six studies used an experimental research design and long-term evaluation.

Conclusions and implication

This systematic review⁵⁴ provides initial knowledge for the development of nursing interventions based on the factors related to loss of appetite in postoperative cardiac surgery patients. Clinical assessment by nurses and other health professionals should include whether patients were on the heart-lung machine ≥ 120 minutes, had emergency surgery, reported having a low cardiac output syndrome, or required mechanical ventilation ≥ 96 hours. To promote patient's nutritional status, there

should be evidence-based practice guidelines on the management of postoperative symptoms related to loss of appetite. These would include pain management, treatment of constipation, and reduction of emotional stress and depression. Additional information on self-care should be given to patients and families before hospital discharge to relieve their stress and depression, enhance knowledge of nutrition to promote healing, and prevent loss of appetite. However, nurses and health professionals should first assess health literacy to ensure that patients and families adequately understand the discharge instructions. Discharge planning should provide instruction on how to support self-care ability and reduce post-discharge problems, especially guidance in nutrition after coronary artery bypass graft surgery. A multidisciplinary approach, including physician, nurse, dietitian/nutritionist, and pharmacist, should be considered as part of the holistic care given to postoperative cardiac surgery patients because loss of appetite can result from multiple factors that lead to poor nutrition and inhibit healing.

Future research should focus on the identified factors related to appetite loss in postoperative cardiac surgery patients. The use of multiple research methods and longitudinal studies will provide a foundation for evidence-based interventions to reduce loss of appetite and improve nutritional status for patients after cardiac surgery.

Data availability

Underlying data

All data underlying the results are available as part of the article and no additional source data are required.

Reporting guidelines

Figshare: PRISMA checklist for 'Factors related to loss of appetite in postoperative cardiac surgery patients: A systematic review', <https://doi.org/10.6084/m9.figshare.14473188>⁵⁴

Data are available under the terms of the Creative Commons Zero "No rights reserved" data waiver (CC0 1.0 Public domain dedication).

Acknowledgements

We are very thankful to those who contributed to this systematic review for their collaboration and support. Special appreciation is extended to Dr. Andrew C. Mills for reviewing early drafts.

References

- American Heart Association: **Heart disease and stroke statistics 2019 update: A report from the American Heart Association**. *Circulation*. 2019; **139**(10): e56–e528.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Cohn LH, Adams DH: **Cardiac surgery in the adult (5th edition)**. McGraw Hill Education, 2016.
[Reference Source](#)
- Zubrzycki M, Liebold A, Skrabal C, et al.: **Assessment and pathophysiology of pain in cardiac surgery**. *J Pain Res*. 2018; **11**: 1599–1611.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
- Murphy GJ, Angelini GD: **Side effects of cardiopulmonary bypass: What is the reality?** *J Card Surg*. 2004; **19**(6): 481–488.
[PubMed Abstract](#) | [Publisher Full Text](#)
- Gaudriot B, Uhel F, Gregoire M, et al.: **Immune dysfunction after cardiac**

- surgery with cardiopulmonary bypass: Beneficial effects of maintaining mechanical ventilation.** *Shock*. 2015; **44**(3): 228–233.
[PubMed Abstract](#) | [Publisher Full Text](#)
6. Knapik P, Nadziakiewicz P, Urbanska E, *et al.*: **Cardiopulmonary bypass increases postoperative glycemia and insulin consumption after coronary surgery.** *Ann Thorac Surg*. 2009; **87**(6): 1859–1865.
[PubMed Abstract](#) | [Publisher Full Text](#)
 7. Khamsiri N, Wanitkun N, Sindhu S, *et al.*: **The relationship between blood loss, systemic inflammatory response syndrome, blood glucose, pain, and recovery in patients during the first 12 hours after open heart surgery.** *Thai Journal of Cardio-Thoracic Nursing*. 2012; **23**(1): 2–18.
[Reference Source](#)
 8. Ścisło L, Bizoń A, Walewska E, *et al.*: **Nutritional status of elderly patients after coronary artery bypass surgery.** *Int J Environ Res Public Health*. 2019; **16**(2): 226.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
 9. Gao M, Sun J, Young N, *et al.*: **Impact of Body Mass Index on Outcomes in Cardiac Surgery.** *J Cardiothorac Vasc Anesth*. 2016; **30**(5): 1308–1316.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
 10. Chermesh I, Hajos J, Mashiach T, *et al.*: **Malnutrition in cardiac surgery: Food for thought.** *Eur J Prev Cardiol*. 2014; **21**(4): 475–483.
[PubMed Abstract](#) | [Publisher Full Text](#)
 11. Ringaitienė D, Gineitytė D, Vicka V, *et al.*: **Preoperative risk factors of malnutrition for cardiac surgery patients.** *Acta Med Lit*. 2019; **23**(2): 99–109.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
 12. Aromataris E, Munn Z: **Joanna Briggs Institute Reviewer's Manual**. 2018.
 13. Schünemann H, Brożek J, Guyatt G, *et al.*: **Handbook for grading the quality of evidence and the strength of recommendations using the GRADE approach.** GRADE handbook (grade.pro.org). 2020.
[Reference Source](#)
 14. Ammouri AA, Al-Daakak ZM, Isac C, *et al.*: **Symptoms experienced by Jordanian men and women after coronary artery bypass graft surgery.** *Dimens Crit Care Nurs*. 2016; **35**(3): 125–132.
[PubMed Abstract](#) | [Publisher Full Text](#)
 15. Corrêa CG, Cruz DA: **Pain: Clinical validation with postoperative heart surgery patients.** *Nurs Diagn*. 2000; **11**(1): 5–14.
[PubMed Abstract](#) | [Publisher Full Text](#)
 16. Grap MJ, Savage L, Ball GB: **The incidence of gastrointestinal symptoms in cardiac surgery patients through six weeks after discharge.** *Heart Lung*. 1996; **25**(6): 444–450.
[PubMed Abstract](#) | [Publisher Full Text](#)
 17. King KB, Parrinello KA: **Patient perceptions of recovery from coronary artery bypass grafting after discharge from the hospital.** *Heart Lung*. 1998; **17**(6 Pt 1): 708–15.
[PubMed Abstract](#)
 18. Miller KH, Grindel CG: **Comparison of symptoms of younger and older patients undergoing coronary artery bypass surgery.** *Clin Nurs Res*. 2004; **13**(3): 179–93; discussion 194–8.
[PubMed Abstract](#) | [Publisher Full Text](#)
 19. Zhang G, Wu N, Liu H, *et al.*: **Case control study of gastrointestinal complications after cardiopulmonary bypass heart surgery.** *Perfusion*. 2009; **24**(3): 173–178.
[PubMed Abstract](#) | [Publisher Full Text](#)
 20. Muangpaisan W (Ed.): **Gerontology and geriatrics for primary care practice.** *Thai Society of Gerontology and Geriatric Medicine*. 2017.
 21. Landi F, Calvani R, Tosato M, *et al.*: **Anorexia of aging: Risk factors, consequences, and potential treatments.** *Nutrients*. 2016; **8**(2): 69.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
 22. Galassetti P: **Inflammation and oxidative stress in obesity, metabolic syndrome, and diabetes.** *Exp Diabetes Res*. 2012; **2012**: 943706.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
 23. Hansson GK: **Inflammation, atherosclerosis, and coronary artery disease.** *N Engl J Med*. 2005; **352**(16): 1685–1695.
[PubMed Abstract](#) | [Publisher Full Text](#)
 24. Cebeci F, Celik SS: **Discharge training and counselling increase self-care ability and reduce postdischarge problems in coronary artery bypass graft surgery patients.** *J Clin Nurs*. 2008; **17**(3): 412–420.
[PubMed Abstract](#) | [Publisher Full Text](#)
 25. Choocherd S, Wanitkun N, Danaidusadeekul S, *et al.*: **Relationships among health literacy, severity of disease, patient engagement, perception of person-centered care and quality of life in patients after coronary artery bypass graft surgery.** *Journal of Nursing Science*. 2016; **34**(1): 94–106.
[Reference Source](#)
 26. Eghbalzadeh K, Sabashnikov A, Weber C, *et al.*: **Impact of preoperative elevated serum creatinine on long-term outcome of patients undergoing aortic repair with Stanford A dissection: A retrospective matched pair analysis.** *Ther Adv Cardiovasc Dis*. 2018; **12**(11): 289–298.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
 27. Rettig TCD, Peelen LM, Geuzebroek GSC, *et al.*: **Impact of intraoperative hypotension during cardiopulmonary bypass on acute kidney injury after coronary artery bypass grafting.** *J Cardiothorac Vasc Anesth*. 2017; **31**(2): 522–528.
[PubMed Abstract](#) | [Publisher Full Text](#)
 28. de Oliveira Sá MPB, Nogueira JRC, Ferraz PE, *et al.*: **Risk factors for low cardiac output syndrome after coronary artery bypass grafting surgery.** *Rev Bras Cir Cardiovasc*. 2012; **27**(2): 217–223.
[PubMed Abstract](#)
 29. Kang J, Yun S, Cho YS, *et al.*: **Post-intensive care unit depression among critical care survivors: A nationwide population-based study.** *Jpn J Nurs Sci*. 2020; **17**(2): e12299.
[PubMed Abstract](#) | [Publisher Full Text](#)
 30. Lawson EA, Holsen LM, Desanti R, *et al.*: **Increased hypothalamic-pituitary-adrenal drive is associated with decreased appetite and hypoactivation of food-motivation neurocircuitry in anorexia nervosa.** *Eur J Endocrinol*. 2013; **169**(5): 639–647.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
 31. Zakkar M, Guida G, Suleiman MS, *et al.*: **Cardiopulmonary bypass and oxidative stress.** *Oxid Med Cell Longev*. 2015; **2015**: 189863.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
 32. Mitchell JD, Grocott HP, Phillips-Bute B, *et al.*: **Cytokine secretion after cardiac surgery and its relationship to postoperative fever.** *Cytokine*. 2007; **38**(1): 37–42.
[PubMed Abstract](#) | [Publisher Full Text](#)
 33. Schumer EM, Chaney JH, Trivedi JR, *et al.*: **Emergency coronary artery bypass grafting: Indications and outcomes from 2003 through 2013.** *Tex Heart Inst J*. 2016; **43**(3): 214–219.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
 34. Pignay-Demaria V, Lespérance F, Demaria RG, *et al.*: **Depression and anxiety and outcomes of coronary artery bypass surgery.** *Ann Thorac Surg*. 2003; **75**(1): 314–321.
[PubMed Abstract](#) | [Publisher Full Text](#)
 35. Bootsatham N, Vanichkul N, Sindhu S, *et al.*: **The relationships among serum creatinine level, ejection fraction, depression, cardio pulmonary bypass time, physical condition and extubation time in patients with elective open heart surgery.** *Journal of the Royal Thai Army Nurses*. 2016; **17**(3): 115–122.
[Reference Source](#)
 36. Kyle Simmons W, Burrows K, Avery JA, *et al.*: **Depression-related increases and decreases in appetite: dissociable patterns of aberrant activity in reward and interoceptive neurocircuitry.** *Am J Psychiatry*. 2016; **173**(4): 418–428.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
 37. Simmons WK, Burrows K, Avery JA, *et al.*: **Appetite changes reveal depression subgroups with distinct endocrine, metabolic, and immune states.** *Mol Psychiatry*. 2020; **25**(7): 1457–1468.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
 38. Jayakumara S, Borrelli M, Milan Z, *et al.*: **Optimizing pain management protocols following cardiac surgery: A protocol for a national quality improvement study.** *Int J Surg Protoc*. 2019; **14**: 1–8.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
 39. Owayolu Ö, Owayolu N, Aytaç S, *et al.*: **Pain in cancer patients: Pain assessment by patients and family caregivers and problems experienced by caregivers.** *Support Care Cancer*. 2015; **23**(7): 1857–1864.
[PubMed Abstract](#) | [Publisher Full Text](#)
 40. Paulsen Ø, Laird B, Aass N, *et al.*: **The relationship between pro-inflammatory cytokines and pain, appetite and fatigue in patients with advanced cancer.** *PLoS One*. 2017; **12**(5): e0177620.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
 41. Zhang JM, An J: **Cytokines, inflammation and pain.** *Int Anesthesiol Clin*. 2007; **45**(2): 27–37.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
 42. Grunkemeier DM, Cassara JE, Dalton CB, *et al.*: **The narcotic bowel syndrome: clinical features, pathophysiology, and management.** *Clin Gastroenterol Hepatol*. 2007; **5**(10): 1126–1139, quiz 1121–2.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
 43. Wiffen PJ, Derry S, Moore RA: **Impact of morphine, fentanyl, oxycodone or codeine on patient consciousness, appetite and thirst when used to treat cancer pain.** *Cochrane Database Syst Rev*. 2014; **2014**(5): CD011056.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
 44. Van der Schaaf M, Vermeulen H, Storm-Versloot MN, *et al.*: **Effectiveness of lactulose syrup after cardiac surgery.** *Appl Nurs Res*. 2004; **17**(1): 48–54.
[PubMed Abstract](#) | [Publisher Full Text](#)
 45. Lainscak M, Blue L, Clark AL, *et al.*: **Self-care management of heart failure: Practical recommendations from the patient care committee of the heart failure association of the European society of cardiology.** *Eur J Heart Fail*. 2011; **13**(2): 115–126.
[PubMed Abstract](#) | [Publisher Full Text](#)
 46. Andrae C, Strömberg A, Arestedt K: **Prevalence and associated factors for decreased appetite among patients with stable heart failure.** *J Clin Nurs*. 2016; **25**(11–12): 1703–1712.
[PubMed Abstract](#) | [Publisher Full Text](#)
 47. Punniyakotti S, Begum B, Kumar A: **A case report on digoxin intoxication in a clinical pharmacist's perspective.** *Asian Journal of Pharmaceutical and Clinical Research*. 2018; **11**(4): 18.
[Publisher Full Text](#)
 48. Davis KD, Cheng JC: **Differentiating trait pain from state pain: A window into brain mechanisms underlying how we experience and cope with pain.** *Pain Rep*. 2019; **4**(4): e735.
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
 49. Leal PC, Goes TC, Ferreira da Silva LC, *et al.*: **Trait vs. state anxiety in different**

threatening situations. *Trends Psychiatry Psychother.* 2017; **39**(3): 147–157.
[PubMed Abstract](#) | [Publisher Full Text](#)

50. Dietz TM, Lisbeth U: **The surgical hospital patient's nutritional risks: A literature review.** *Klinisk Sygepleje.* 2012; **26**: 9–22.
51. Mignini EV, Scarpellini E, Rinninella E, *et al.*: **Impact of patients nutritional status on major surgery outcome.** *Eur Rev Med Pharmacol Sci.* 2018; **22**(11): 3524–3533.
[PubMed Abstract](#) | [Publisher Full Text](#)
52. Makaronidis JM, Neilson S, Cheung W, *et al.*: **Reported appetite, taste and smell changes following Roux-en-Y gastric bypass and sleeve gastrectomy:**

Effect of gender, type 2 diabetes and relationship to post-operative weight loss. *Appetite.* 2016; **107**: 93–105.
[PubMed Abstract](#) | [Publisher Full Text](#)

53. Bryant EJ, Malik MS, Whitford-Bartle T, *et al.*: **The effects of bariatric surgery on psychological aspects of eating behaviour and food intake in humans.** *Appetite.* 2020; **150**: 104575.
[PubMed Abstract](#) | [Publisher Full Text](#)
54. Figshare: **PRISMA checklist for 'Factors related to loss of appetite in postoperative cardiac surgery patients: A systematic review'.**
<http://www.doi.org/10.6084/m9.figshare.14473188>

Open Peer Review

Current Peer Review Status: ?

Version 1

Reviewer Report 13 September 2021

<https://doi.org/10.5256/f1000research.55541.r92460>

© 2021 Ji B. This is an open access peer review report distributed under the terms of the [Creative Commons Attribution License](#), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Bingyang Ji

Department of Cardiopulmonary Bypass, State Key Laboratory of Cardiovascular Medicine, Fuwai Hospital, National Center for Cardiovascular Disease, Chinese Academy of Medical Sciences, Beijing, China

The authors systematically reviewed the factors related to appetite loss after cardiac surgery, which is a quite interesting topic. I have several suggestions:

- The INTRODUCTION section introduced background knowledge of cardiac surgery. I think the authors should discuss less about it and merge this part with the BACKGROUND section.
- I have some concerns on the methods of systematic review. The authors listed PRISM flowchart, some important data were not reported. After excluding duplications, 3246 articles were excluded because they were not published in English/Thai, did not report heart surgery patients or other reasons. The authors should better report the exact number of patients excluded in every step. This may allow replication by other researchers.
- Table 2 reported **Quality Assessment of the Evidence by GRADE Guideline**, and all six articles were of high or moderate quality. I suggest the authors reported more details on assessing the article. It's better to not just report whether it is precise, but report the details of how you decide it's precise.
- I recommend the authors to ask for language editing, as some syntax errors existed. e.g. Page 6, Paragraph 4, Line 6, 'Pain is both a rapidly (state variable) and slowly (trait variable) changing factor. '

Are the rationale for, and objectives of, the Systematic Review clearly stated?

Partly

Are sufficient details of the methods and analysis provided to allow replication by others?

Partly

Is the statistical analysis and its interpretation appropriate?

Yes

Are the conclusions drawn adequately supported by the results presented in the review?

Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: The blood conservation and organ protection during cardiopulmonary bypass. Improving the prognosis of extracorporeal life support.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Author Response 28 Sep 2021

Samoraphop Banharak, Faculty of Nursing, Khon Kaen University, Khon Kaen, Thailand

- *The INTRODUCTION section introduced background knowledge of cardiac surgery. I think the authors should discuss less about it and merge this part with the BACKGROUND section.*
- **Response:** Thank you for suggestion. The introduction and Background to an academic paper are different things and both are essential. The Introduction comes first and is a relatively short section of the manuscript which sets the study we are reporting in its widest context. However, the Background is the place to begin to focus on what, specifically, we investigated. In other words, the INTRODUCTION is the overview, however, BACKGROUND is more scope and focus of what is the phenomenon of this study. For these reasons, we would like to separate and keep these two parts if possible.
- *I have some concerns on the methods of systematic review. The authors listed PRISM flowchart, some important data were not reported. After excluding duplications, 3246 articles were excluded because they were not published in English/Thai, did not report heart surgery patients or other reasons. The authors should better report the exact number of patients excluded in every step. This may allow replication by other researchers.*
- **Response:** We would like to say thanks for this useful comment and agree with this suggestion. We can add more detail about how many articles were excluded for each reason. There were 347 for not published in English/Thai; 1,245 not heart surgery patients; 109 animal study; and 1,545 not research article.
- *Table 2 reported Quality Assessment of the Evidence by GRADE Guideline, and all six articles were of high or moderate quality. I suggest the authors reported more details on assessing the article. It's better to not just report whether it is precise, but report the details of how you decide it's precise.*
- **Response:** Thank you so much for useful suggestion. We have followed the GRADE Guideline from Joanna Briggs Institute and provide the standard reported table of

GRADE following "Quality Assessment of the Evidence by GRADE Guideline." However, we can add more detail about the reason for giving score for risk of bias, precision, directness, and consistency at the Table 2.

- Unclear = The researchers did not indicate or reported how they designed for controlling confounding factors and dealing with missing data
 - Precise = The researchers described how to measure their primary and secondary outcomes and used appropriate statistic for their data analysis
 - Direct = The researchers demonstrated they measured primary and secondary outcomes in intervention and control groups in the same way
 - Consistent = The researchers demonstrated they measured primary and secondary outcomes in intervention and control groups in the same construct and measurement
-
- *I recommend the authors to ask for language editing, as some syntax errors existed. e.g. Page 6, Paragraph 4, Line 6, 'Pain is both a rapidly (state variable) and slowly (trait variable) changing factor.'*
 - **Response:** Thank you so much for suggestion. We have edited this sentence as "Pain is both a rapid (state variable) and slow (trait variable) changing factor." Moreover, this manuscript will be proved again by the English native speaker before publishing the final version.

Competing Interests: Non-Financial Competing Interests

The benefits of publishing with F1000Research:

- Your article is published within days, with no editorial bias
- You can publish traditional articles, null/negative results, case reports, data notes and more
- The peer review process is transparent and collaborative
- Your article is indexed in PubMed after passing peer review
- Dedicated customer support at every stage

For pre-submission enquiries, contact research@f1000.com

F1000Research