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Review Stage at time of this submission: Completed but not published.

Conflicts of interest: None declared.

INTRODUCTION

Review question / Objective: This study reviews the current evidence on clinical characteristics and outcome of Acute Pancreatitis following spinal surgery.

Rationale: Acute pancreatitis is a known postoperative complication in many

abdominal as well as extra abdominal surgeries 1-5. Postoperative pancreatitis is associated with a higher risk of local and systemic complications with high morbidity and mortality rates 6. The severity of pancreatitis ranges from mild to severe with increasing mortality seen in patients with severe pancreatitis, necrotizing pancreatitis and multi-organ failure 7. In

Clinical characteristics and outcomes of acute pancreatitis following spinal surgery: a systematic review

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Review question / Objective: This study reviews the current evidence on clinical characteristics and outcome of Acute Pancreatitis following spinal surgery.

Condition being studied: Acute pancreatitis in spinal surgery. Information sources: All articles were searched electronically using PubMed/Medline, Scopus, EMBASE, Cochrane CENTRAL, and Latin American & Caribbean Health Sciences Literature (LILACS) before May 2020 without any restriction in the language or status of publication. Key words related to acute pancreatitis and its complications and various types of spinal surgeries were searched in the title and abstract fields.

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 05 July 2022 and was last updated on 05 July 2022 (registration number INPLASY202270017).

INPLASY

patients with post-operative pancreatitis, the mortality rate has been reported to be up to 50% 8. Although the incidence of postoperative pancreatitis is low, routinely monitoring with clinical and biochemical parameters helps facilitate early diagnosis and treatment especially among patients undergoing surgeries with a known high risk of pancreatitis . The literature available on acute pancreatitis following spinal surgery is limited. Therefore, we conducted this systematic review to describe the clinical characteristics, risk factors and outcomes of acute pancreatitis among patients undergoing spinal surgeries.

Condition being studied: Acute pancreatitis in spinal surgery.

METHODS

Search strategy:

PubMed, Embase (Elsevier), LILACS, Scopus (Elsevier) and Cochrane CENTRAL were included in the search strategy. The searches were performed from inception to May 15,2020.

PubMed

((((("acute pancreatitis" [MeSH Terms]) OR "necrotizing pancreatitis" [MeSH Terms]) OR "hemorrhagic pancreatitis"[MeSH Terms]) OR "pancreatic pseudocyst "[MeSH Terms]) OR ('pancreatitis')) AND ((((((("minimally invasive anterior stabilization" [MeSH Terms]) OR "minimally invasive posterior short segment fixation" [MeSH Terms]) OR "posterior short segment fixation" [MeSH Terms]) OR "open reduction and internal fixation" [MeSH Terms]) OR "iliosacral screw fixation" [MeSH Terms]) OR "spinopelvic fixation" [MeSH Terms]) OR "trans-pedicular screw fixation" [MeSH Terms]) OR "discectomy" [MeSH Terms]) OR "laminectomy and decompression" [MeSH Terms]) OR "transforaminal lumbar interbody fusion" [MeSH Terms]) OR "vertebroplasty/ kyphoplasty" [MeSH Terms]) OR "posterior instrumentation for scoliosis" [MeSH Terms]) OR "spinal surgery" [MeSH Terms]) OR "scoliosis surgery" [MeSH Terms])) Limit: From Inception to 15 May 2020 **Embase (Elsevier)**

('acute pancreatitis'/exp OR 'necrotizing pancreatitis'/exp OR 'hemorrhagic pancreatitis'/exp OR 'pancreatic pseudocyst'/exp OR ' pancreatitis') AND ('minimally invasive anterior stabilization'/ exp OR 'minimally invasive posterior short segment fixation'/exp OR 'posterior short segment fixation'/exp OR 'open reduction and internal fixation'/exp OR 'iliosacral screw fixation'/exp OR 'spinopelvic fixation'/exp OR 'trans-pedicular screw fixation'/exp OR 'discectomy'/exp OR 'laminectomy and decompression'/exp OR 'transforaminal lumbar interbody fusion'/ exp OR 'vertebroplasty/ kyphoplasty'/exp OR 'posterior instrumentation for scoliosis'/exp OR 'spinal surgery'/exp OR 'scoliosis surgery'/exp) AND [embase]/lim NOT ([embase]/lim AND [medline]/lim Limit: From Inception to 15 May 2020 Latin American and Caribbean Center on Health Sciences Information (LILACS) (MH:("acute pancreatitis") OR ("necrotizing pancreatitis") OR ("hemorrhagic pancreatitis") OR ("pancreatic pseudocyst") OR ("pancreatitis")) AND (MH: ("minimally invasive anterior stabilization") OR ("minimally invasive posterior short segment fixation") OR ("posterior short segment fixation") OR ("open reduction and internal fixation") OR ("iliosacral screw fixation") OR ("spinopelvic fixation") OR ("trans-pedicular screw fixation") OR ("discectomy") OR ("laminectomy and decompression") OR ("transforaminal lumbar interbody fusion") OR ("vertebroplasty/ kyphoplasty") OR ("posterior instrumentation for scoliosis") OR ("spinal surgery") OR ("scoliosis surgery")

Limit: From Inception to 15 May 2020 Scopus (Elsevier)

("acute pancreatitis" OR "necrotizing pancreatitis" OR "hemorrhagic pancreatitis" OR "pancreatic pseudocyst" OR "pancreatitis") AND ("minimally invasive anterior stabilization" OR "minimally invasive posterior short segment fixation" OR "posterior short segment fixation" OR "open reduction and internal fixation" OR "iliosacral screw fixation" OR "spinopelvic fixation" OR "trans-pedicular screw fixation" OR "discectomy" OR "laminectomy and decompression" OR

"posterior instrumentation for scoliosis" OR "spinal surgery" OR "scoliosis surgery") Limit: From Inception to 15 May 2020 AND **NOT INDEX(medline)** Cochrane CENTRAL (MeSH descriptor: [acute pancreatitis] explode all trees OR MeSH descriptor: [necrotizing pancreatitis] explode all trees **OR MeSH descriptor:** [hemorrhagic pancreatitis] explode all trees OR MeSH descriptor: [pancreatic pseudocyst] explode all trees OR MeSH descriptor: [pancreatitis] explode all trees OR acute pancreatitis * OR necrotizing pancreatitis * OR hemorrhagic pancreatitis * OR pancreatic pseudocyst * OR pancreatitis *) AND (MeSH descriptor: [minimally invasive anterior stabilization] explode all trees OR MeSH descriptor: [minimally invasive posterior short segment fixation] explode all trees OR MeSH descriptor: [posterior short segment fixation] explode all trees OR MeSH descriptor: [open reduction and internal fixation] explode all trees OR MeSH descriptor:[iliosacral screw fixation] explode all trees OR MeSH descriptor: [spinopelvic fixation] explode all trees OR MeSH descriptor: [trans-pedicular screw fixation] explode all trees OR MeSH descriptor: [discectomy] explode all trees **OR MeSH descriptor:** [laminectomy and decompression] explode all trees OR MeSH descriptor:[transforaminal lumbar interbody fusion] explode all trees OR MeSH descriptor: [vertebroplasty/ kyphoplasty] explode all trees OR MeSH descriptor: [posterior instrumentation for scoliosis] explode all trees OR MeSH descriptor:[spinal surgery] explode all trees OR MeSH descriptor: [scoliosis surgery] explode all trees OR minimally invasive anterior stabilization * OR minimally invasive posterior short segment fixation* OR posterior short segment fixation * OR posterior short segment fixation * OR open reduction and internal fixation * OR iliosacral screw fixation * OR spinopelvic fixation * OR trans-pedicular screw fixation * OR discectomy * OR laminectomy and decompression * OR transforaminal lumbar interbody fusion * OR vertebroplasty/

"transforaminal lumbar interbody fusion"

OR "vertebroplasty/ kyphoplasty" OR

kyphoplasty * OR posterior instrumentation for scoliosis * OR spinal surgery * OR scoliosis surgery *)

Limit: Publication date Inception to May 2020.

Participant or population: Patients with a diganosis of acute pancreatitis following spinal surgery.

Intervention: None.

Comparator: None.

Study designs to be included: Systematic review according to PRISMA guidelines.

Eligibility criteria: Inclusion criteria was defined as studies describing patients with at least 2 out of 3 criteria of acute pancreatitis after any spinal surgery.

Information sources: All articles were searched electronically using PubMed/ Medline, Scopus, EMBASE, Cochrane CENTRAL, and Latin American & Caribbean Health Sciences Literature (LILACS) before May 2020 without any restriction in the language or status of publication. Key words related to acute pancreatitis and its complications and various types of spinal surgeries were searched in the title and abstract fields.

Main outcome(s): Eleven papers (including 6 case reports) were included, with 306 patients (with an incidence of 23.0%) developing AP in patients undergoing spinal surgery (mean age= 14.2 years). Of the studies that specified symptoms (n=55 patients), abdominal pain (43.6%), nausea and vomiting (32.7%) and abdominal distension (7.27%) were the commonest. The mean duration from surgery to onset of symptoms was 6.15 days (range:1-7). Almost all (n=10, 90.9%) were treated nonoperatively. Of the complications mentioned (n=306 patients), glucose intolerance (25%), peritonitis (2%), pseudocyst (2%), and fluid collection (2%) were the commonest. Prolonged fasting time (13.6%), intra-operative blood loss (9.09%), gastroesophageal reflux disease (9.1%), age >14 years (9.1 %), and low BMI

(9.1 %) were the commonest associated factors for AP. A total of 2 deaths (n=2/306, 0.6%) were reported.

Additional outcome(s): Clinical symptoms and signs

Of the studies that specified symptoms (n=55), abdominal pain (43.6%, n=24/55), nausea and vomiting (32.7%, n=18/55), and abdominal distention (7.3%, n=4/55) were the commonest. The other features described included reduced bowel sounds 5.4% (n=3/55), food intolerance 3.6% (n=2/55) and prolong ileus 3.6% (n=2/55). These clinical features appeared following a mean duration of 6.1 days after surgery (Table 1).

Biochemical findings

Only studies having a serum amylase elevation of more than three times the upper limit of normal were included therefore all studies and case reports showed an elevation of serum amylase. However, an elevation of serum lipase was observed in 65% (n=199/306) patients (Table 2).

Imaging findings Only studies which included definitive imaging evidence of acute pancreatitis were included. Although, all studies and case reports included imaging findings inclusive of 306 total patients, only 24.5% (n=75/306) patients had a detailed reporting of imaging. Of these 61 patients, 81.3% (n=61/75) underwent an abdominal ultrasound scan and the rest 18.6% (n=14/75) underwent a CT (Table 2).

Treatment used

All except one patient were treated nonoperatively keeping nil by mouth with nasogastric suction, intravenous fluids, administration of somatostatin and intravenous antibiotic prophylaxis until clinical improvement was observed. Four patients were given total parenteral nutrition and one patient needed total parenteral nutrition. One patient underwent surgery for corporeal fracture of the pancreas post surgically after correction of the spinal deformity (Table 3).

Risk factors

A total of three studies described prolonged fasting time (13.6%), intraoperative blood loss (9.1%), gastroesophageal reflux disease (9.1%), age >14 years (9.1%), low BMI (9.1%), and anterior approach and combined approach (9.1%) as the most common risk factors. Risk factors such as duration of surgery, total parenteral nutrition, feeding difficulty, reactive airway disease, increased TNF alpha level, urine trypsin-associated peptide levels, male sex, gastrointestinal tube, reactive.

Quality assessment / Risk of bias analysis: The risk of bias assessment of eligible studies was performed using the Downs and Black checklist which is both a valid and a reliable tool to assess both randomised and non-randomised control studies (external validity KR20:0.54, internal consistency KR-20:0.8914).

Strategy of data synthesis: Initial screening for eligibility was performed by two investigators based on the titles, abstracts, and keywords of citations from electronic databases. Thereafter, full texts of all relevant records were assessed based on the inclusion criteria. In doubtful situations. the consensus was arrived after the input from the senior authors. All data pertaining to the clinical presentation, risk factors, investigations, treatment and outcomes were extracted, categorised and tabulated. Finally, qualitative analysis was performed with the available data. A meta-analysis could not be performed due to the heterogeneity in the study methodology, treatment options and description of outcomes. The analysis was in keeping with the PRISMA guidelines.

Subgroup analysis: Initial screening for eligibility was performed by two investigators based on the titles, abstracts, and keywords of citations from electronic databases. Thereafter, full texts of all relevant records were assessed based on the inclusion criteria. In doubtful situations, the consensus was arrived after the input from the senior authors. All data pertaining to the clinical presentation, risk factors, investigations, treatment and outcomes were extracted, categorised and tabulated. Finally, qualitative analysis was performed with the available data. A meta-analysis could not be performed due to the heterogeneity in the study methodology, treatment options and description of outcomes.

Sensitivity analysis: A systematic review of all studies on pancreatitis following spinal surgeries including prospective and retrospective cohort analysis and experimental studies was performed. Due to the limited number of studies, we decided to include case reports in this review. Inclusion criteria was defined as studies describing patients with at least 2 out of 3 criteria of acute pancreatitis after any spinal surgery. The primary objective was to describe the clinical characteristics. risk factors and outcome of acute pancreatitis following spinal surgeries. We also aimed to describe attempted treatment modalities and their outcomes where relevant. The methodology of this review followed the PRISMA recommendations.

Search strategy All articles were searched electronically using PubMed/Medline, Scopus, EMBASE, Cochrane CENTRAL, and Latin American & Caribbean Health Sciences Literature (LILACS) before May 2020 without any restriction in the language or status of publication. Key words related to acute pancreatitis and its complications and various types of spinal surgeries were searched in the title and abstract fields. The detailed search strategy is shown in the supplementary file (Annexure 1). Furthermore, the list of references of eligible articles were manually searched and relevant articles were added to the review. Initial screening for eligibility was performed by two investigators based on the titles, abstracts, and keywords of citations from electronic databases. Thereafter, full texts of all relevant records were assessed based on the inclusion criteria. In doubtful situations, the consensus was arrived after the input from the senior authors. All data pertaining to the clinical presentation, risk factors, investigations, treatment and outcomes were extracted, categorised and tabulated. Finally, qualitative analysis was performed with the available data. A meta-analysis could not be performed due to the heterogeneity in the study methodology, treatment options and description of outcomes.

Language: No restriction.

Country(ies) involved: Sri Lanka.

Keywords: Acute pancreatitis, Spinal surgery, Scoliosis, Systematic review.

Dissemination plans: Publication in international journals.

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RJ, SR and UJ, CK contributed to concept and design of study, acquisition of data, analysis, interpretation of data, drafting the article and final approval of the version to be published. SS contributed to concept and design of study, revising it critically for important intellectual content; and final approval.