Review

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Chemotherapy-associated pneumoperitoneum in cancer patients: a scoping review

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Background: The presence of air in the peritoneal cavity (pneumoperitoneum) is often secondary to perforated viscus. Emergent operative intervention is typically warranted in non-cancer patients. Cancer patients present a unique challenge as they have an increased risk of pneumoperitoneum due to local tumour invasion, radiation therapy, and frequent endoscopic procedures. There is a paucity of literature on the management of patients undergoing chemotherapy who present with pneumoperitoneum. The authors conducted a scoping review to identify and synthesize preliminary evidence on the presentation, management, and outcomes of this patient population.

Materials and methods: A scoping review of cases of pneumoperitoneum in cancer patients from 1990 to 2022 was conducted using the Arksey and O'Malley five-stage approach. Inclusion criteria were a known diagnosis of cancer, chemotherapy within 6 months of presentation, and imaging confirmation of pneumoperitoneum. The authors' exclusion criteria were cancer diagnosis at the time of presentation, perforation secondary to local cancer invasion, and last chemotherapy session greater than 6 months prior to presentation.

Results: Thirty-four cases (8 paediatric, 26 adults) were identified. The median time from the last chemotherapy treatment to presentation with pneumoperitoneum was 14 days. Twenty-one patients were managed operatively, and 13 were managed non-operatively. The most common source of perforation was multiple sites along the bowel. Thirty-day mortality was 33.3% for the operative cohort and 23.1% for the non-operative group.

Conclusions: Pneumoperitoneum in cancer patients remains a highly morbid condition with a mortality rate of approximately 30%, regardless of the treatment approach. Non-operative management should be pursued whenever possible.

Keywords: bowel perforation, chemotherapy, pneumoperitoneum, scoping review

Introduction

Pneumoperitoneum, the presence of air in the peritoneal cavity, often necessitates emergent surgical exploration in non-cancer patients. In ~85–90% of cases, it is caused by bowel perforation[1,2], whereas the remaining 10–15% of cases are caused by barotrauma, gynaecological insufflation, and retained postoperative or post-procedural air[3]. Radiography remains the gold standard in diagnosing pneumoperitoneum, as evident by the characteristic radiolucency below the diaphragm on chest X-ray or at a superiorly dependent location on abdominal X-ray[1,2]. However, computed tomography (CT) scans are more sensitive, being able to detect not only intraperitoneal free air but also extraluminal air around the entire gastrointestinal tract[3,4].

The management of patients with pneumoperitoneum can generally be divided into operative and non-operative approaches. Operative management usually involves an exploratory laparotomy to identify and repair or resect the source of bowel

HIGHLIGHTS

- Pneumoperitoneum is an infrequent but severe complication of chemotherapy.
- We review the management of patients with chemotherapy-associated pneumoperitoneum.
- The median time from the last chemotherapy to presentation was 14 days.
- The majority of patients were managed operatively.
- Thirty-day mortality was 33.3% for the operative cohort and 23.1% for the non-operative group.
- Important to prioritize non-operative care in this patient population.

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perforation. The non-operative approach involves the use of broad-spectrum antibiotics, bowel rest with nothing per os, the placement of intra-abdominal drains as indicated, or the pursuit of hospice care[5]. Non-operative management is often most appropriate for patients with advanced or metastatic disease, where the risks associated with an operative intervention may outweigh its possible therapeutic benefits[1,6].

In cancer patients, the management of pneumoperitoneum usually requires a meticulous, multidisciplinary approach. Due to local tumour invasion, the need for multiple endoscopic procedures, and, in some cases, radiotherapy, cancer patients are at increased risk of pneumoperitoneum[6]. In addition, the emergent surgical management of cancer patients is complicated by neutropenia and malnutrition, given the fact that these patients are often immunocompromised and/or receiving multiple chemotherapeutic agents[7]. For patients on neoadjuvant chemotherapy, emergent surgery is likely to negatively affect the ability to achieve complete (R0) resection during the required oncological operation.

Despite the known bowel toxicities associated with chemotherapy and immunotherapy, there are very few cases of pneumoperitoneum or bowel perforation in patients undergoing chemotherapy reported in the literature[6,8–10]. There is also a paucity of literature on the presentation, management, and outcomes of patients on chemotherapy who develop pneumoperitoneum. There are currently no consensus management guidelines for this patient population. Given this lack of consensus guidelines, the primary goal and indication of this scoping review was to identify and synthesize preliminary evidence on the presentation, diagnosis, management, and ultimate outcomes of cancer patients who present with pneumoperitoneum while undergoing chemotherapy.

Materials and methods

Search strategy

This scoping review of reported cases of pneumoperitoneum in cancer patients undergoing chemotherapy was conducted using the Arksey and O'Malley five-step methodological framework[11,12]. The review followed the Preferred Reporting Items for Systematic Reviews and Meta-analyses Scoping Review extension (PRISMA-ScR) guidelines[12,13]. Due to the nature of nebulous search terms like "gas" or "air", the search was kept strictly to pneumoperitoneum and chemotherapy keywords. Keywords were combined using Boolean operators "AND/OR" and modified for each database. We searched three databases, MEDLINE/PubMed, Embase, and Scopus, and retained only articles available in English. Six duplicates were identified and removed, and the remaining 424 articles were transferred to Rayyan, a free online application that helps researchers screen and select articles when performing systematic and scoping reviews. The full study protocol has been peer-reviewed and published in accordance with the guidelines for conducting scoping reviews[14].

Eligibility criteria

Articles published between 1990 and 2022 that contained fully described cases or case series were included. The patient criteria for inclusion were a known diagnosis of cancer, chemotherapy within six months of presentation, and imaging confirmation of pneumoperitoneum. The exclusion criteria were a new cancer diagnosis at the time of presentation, perforation secondary to local invasion by the tumour itself, and chemotherapy more than six months prior to presentation.

Article selection and data extraction

The titles and abstracts of all 424 articles exported to Rayyan were evaluated by three independent reviewers under double-blind conditions to select studies relevant to our population, intervention, comparators, and outcomes (Table 1). After unblinding, the reviewers independently evaluated the doubly screened titles/abstracts. Any conflicts were resolved through discussion arbitrated by a fourth reviewer. The second stage involved screening of the full text by three independent reviewers. Demographic data, clinical presentation, oncologic history, management, and 30-day mortality information were extracted from the articles. The quality of included case reports was determined based on history of recent chemotherapy (within the last six months), diagnostic confirmation of pneumoperitoneum (by imaging), cases reported in sufficient detail for comparative purposes, and details on management and outcomes. As this was a scoping review, the study did not require evaluation and approval by our institutional review board.

Results

The Preferred Reporting Item for Systematic Reviews and Meta-Analyses extension for scoping reviews (PRISMA-ScR) was used throughout the review process to guide the screening and reporting[13], as shown in Figure 1. The initial search identified 430 articles. Six duplicates were removed, and title and abstract screening was completed for the remaining 424 articles. After a full review of these articles, 30 met the inclusion criteria.

A total of 34 cases (8 paediatric, 26 adults) of pneumoperitoneum in patients actively undergoing chemotherapy were identified from the 30 articles (Fig. 1 and Table 2). The median age of the adult patients was 63.5 years, while that of the paediatric patients was 11.5 years. The median number of days from the last chemotherapy to symptom onset was 14 days. Diagnosis was made by a plain film in eight patients (23.5%), by computed tomography (CT) in 13 patients (38.2%), and both plain film and CT in 13 patients (38.2%).

Fourteen patients (41.2%) had haematological cancers, while 20 (58.8%) had solid organ malignancies. Of note, 100% of the paediatric patients had haematological cancers, which were also noted in six adult patients (23.1%). The most common adult malignancy was lung cancer (seven patients, 26.9%). The other adult malignancies were ovarian cancer (11.5%), oesophageal cancer (11.5%), colon cancer (7.7%), renal cell carcinoma (7.7%), breast cancer (3.8%), cervical cancer (3.8%), and gastric cancer (3.8%), as shown in Table 2.

Twenty-one patients (61.8%) were managed operatively: 6 of the 8 paediatric patients (75%) and 15 of the 26 adult patients (57.7%). Among all patients who were managed operatively, 7 (33%) were dead by 30 days post-presentation. Thirteen patients were managed non-operatively, 2 paediatric patients (25%) and 11 adult patients (42.3%). Of the patients who were managed non-operatively, 3 (23.1%) were dead 30 days post-presentation. Overall, the 30-day mortality for all patients was 29.4%.

Table 1

Study inclusion and exclusion criteria

Inclusion criteria	Exclusion criteria
Known diagnosis of cancer at the time of presentation	Cancer diagnosis at the time of presentation
Chemotherapy within 6 months of presentation	Perforation secondary to local tumour invasion by the cancer
Imaging confirmation of pneumoperitoneum	Chemotherapy more than 6 months prior to presentation

When operative management was pursued, perforations were found at multiple sites in 28.6% of patients, in the small bowel in 23.8%, the colon in 14.3%, the stomach in 9.5%, and in the appendix in 4.8% of patients (Fig. 2). Interestingly, 4 patients (18.9%) had imaging-confirmed pneumoperitoneum without any identified viscus perforation at the time of surgery. Of note, none of the published cases reported perforation sites in relation to the intra-abdominal primary tumours or previous surgical sites. The 2 paediatric patients managed non-operatively were asymptomatic upon presentation. Of the 11 adult patients managed non-operatively, 5 were asymptomatic, and 3 pursued comfort measures and died shortly afterward. Three of these patients had abdominal symptoms upon presentation; however, they were hemodynamically stable and non-toxic. The non-operative regimen consisted of bowel rest, intravenous antibiotics, and close monitoring with serial abdominal exams and frequent labs. All three of these patients were alive at 30 days post-presentation.

A total of 7 patients (5 adult, 2 paediatric) were asymptomatic upon presentation that is they did not have significant abdominal pain or peritoneal signs. Two of these patients were evaluated in the outpatient setting for complaints of lethargy and bloating[17,28,] while the rest had incidentally found pneumoperitoneum on imaging work-up as part of their cancer management or for evaluation

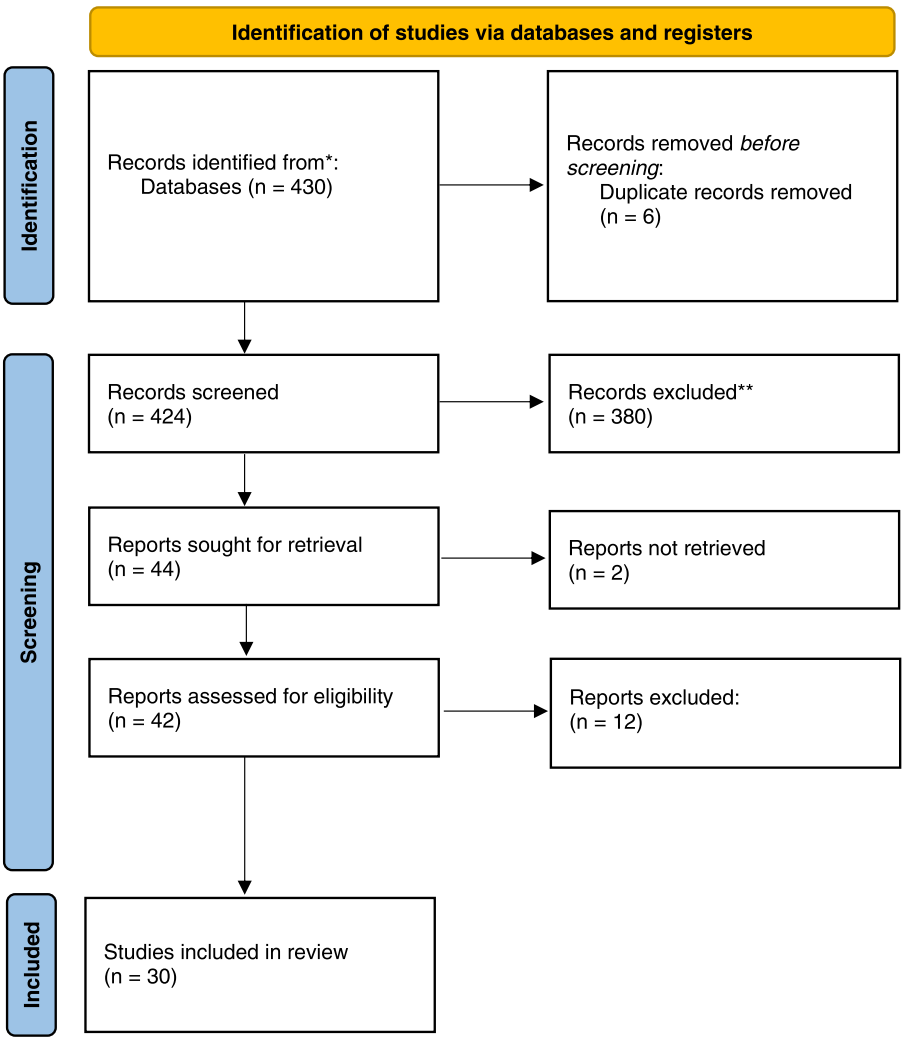

Figure 1. Flow diagram for case reports adopted from Preferred Reporting Items for Systematic Reviews (PRISMA) criteria updated in 2021.

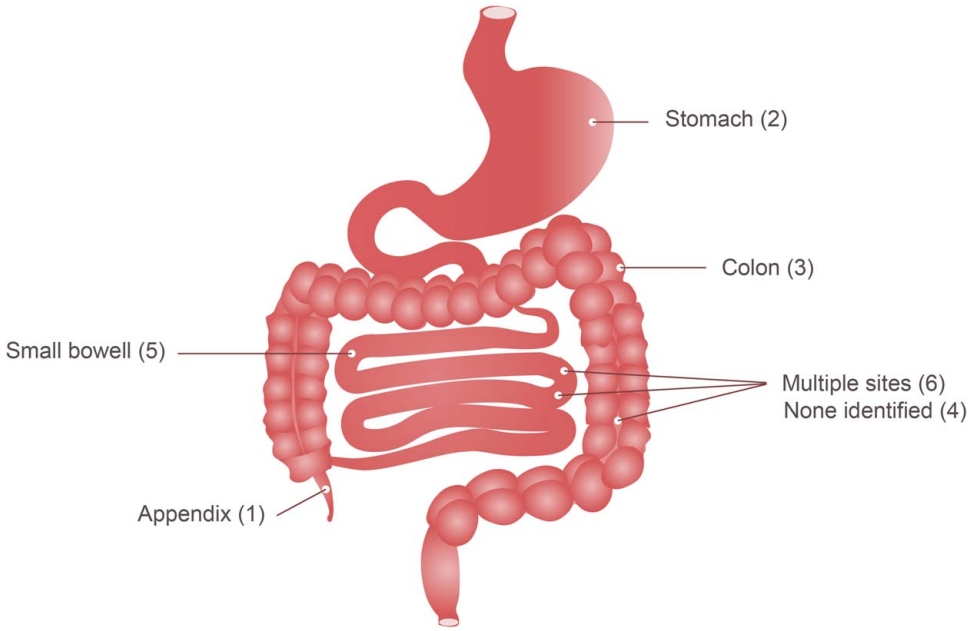

Figure 2. Gastrointestinal perforation sites in patients with chemotherapy-associated pneumoperitoneum.

of non-abdominal complaints[10,22,37,39]. All 7 of these asymptomatic patients were managed non-operatively, and all were alive at 30 days post-presentation.

When surgical management was pursued, the most common type of operation performed was an exploratory laparotomy (76.2%). Laparoscopic surgical intervention was performed in 14.3% of the patients managed operatively, while the type of surgery performed in 9.5% of patients was not specified (Table 3).

The chemotherapy regimens used to treat these patients were grouped into five classes: antimetabolites (AM), anti-tumour antibiotics (ATA), biological response modifiers (BRM), plant alkaloids (PA), and alkylating agents (AA). At the time of presentation, most of the patients were receiving multiple chemotherapy regimens, with only 7 patients (20.6%) being treated with a single agent (Table 2). The patients were treated with these chemotherapeutic agents in the following proportions: PA, 67.6%; AA, 64.7%; BRMs, 38.2%; AMs, 35.3%; and ATA, 32.4% (Table 2). Due to the variety of chemotherapeutic agents, therapeutic regimens, perforation sites, and management options used in these patients, it was not possible to draw correlations between one single agent or regimen and the perforation site or management options. The results are summarized in Table 3.

Discussion

One of the most prevalent complications of chemotherapeutic agents is gastrointestinal side effects. These agents typically act directly on the intestinal mucosa, resulting in oedema and inflammation, which symptomatically manifests as nausea, diarrhoea, constipation, and, in severe cases, enterocolitis, ulcerations, and strictures[42–45]. Bowel perforation is a rare but morbid side effect of chemotherapy. Certain antiangiogenic agents such as aflibercept and bevacizumab have an increased risk of intestinal perforation, with the incidence of perforation being as high as 3% in patients receiving bevacizumab therapy[8,24,26,46,47]. Several mechanisms have been postulated as the cause of gastrointestinal perforation secondary to chemotherapeutic agents. Antiangiogenic agents, in particular, reduce the capillary density of the mucosal layer and compromise intestinal wall integrity, thus increasing the risk of bowel ischaemia and subsequent perforation[48,49]. Other etiologies of bowel perforation include treatment response with tumour lysis or as sequelae of other side effects, most notably pneumatosis intestinalis and enterocolitis[48]. Risk factors associated with bowel perforation and pneumoperitoneum subsequent to chemotherapeutic agent use include a primary gastrointestinal tumour, prior abdominal radiation, peptic ulcer disease, and peritoneal carcinomatosis[6].

In this scoping review, we sought to identify and synthesize the available evidence from published case reports on the presentation, management, and outcomes of patients on chemotherapy who present with pneumoperitoneum. Free intraperitoneal air caused by intestinal perforation usually necessitates emergent surgery, but for patients with non-obstructive and/or metastatic cancers, this diagnosis poses a significant decision-making dilemma. One such predicament is the difficult nature of surgery during ongoing chemotherapy. Although there is currently no consensus on the most appropriate time for surgery after chemotherapy, several studies have shown that fewer surgical complications occur if elective surgery is delayed until four to eight weeks after the completion of neoadjuvant chemotherapy[50–52]. Surgical complications such as poor wound healing, increased risk of infection, and tissue that is generally friable make surgery within the first three weeks of chemotherapy an arduous task with worse patient outcomes[53].

In our study, we found that the median time from the last chemotherapy treatment to presentation with pneumoperitoneum was 14 days, which is a suboptimal time to pursue abdominal surgery. We found that the majority of these

Table 2

Sociodemographic data and clinical presentation of included cases

Ref	Age (year)	Sex (M/F)	Time since last chemotherapy (day)	Type of cancer	Imaging modality	Chemotherapy regimen	Chemotherapy class (es)	Abdominal symptoms (Y/N)	Intervention (operative/non-operative)	Perforation site	30-day status
[15]	2	F	4	PTLD	XR	CHOP	AA, ATA, PA	Y	Op	Small bowel, multiple	Dead
[16]	2	F	33	ALL	XR	VAD	ATA, NP, PA	Y	Op	None	Alive
[17]	3	M	120	ALL	XR + CT	COPADM	PA, ATA, AA, 3 AMs	N	Non	N/A	Alive
[18]	10	M	14	ALL	XR + CT	COPADM	PA, ATA, AA, 3 AMs	Y	Op	Appendix	Alive
[19]	13	M	22	ALL	XR + CT	MTX, V, DRC	AM, PA, ATA	Y	Op	Colon	Alive
[20]	14	M	Unknown	HL	XR	COPADM	PA, ATA, AA, 3 AMs	Y	Op	None	Alive
[21]	14	M	21	EBV-LPD	CT	EPEG	PA	Y	Op	None	Alive
[22]	17	M	Unknown	ALL	XR + CT	VAD	ATA, NP, PA	N	Non	N/A	Alive
[23]	39	F	3	Colon	CT	FOLFOX	AM, AA	Y	Non	N/A	Dead
[24]	43	M	4	NHL	XR	CHOP	AA, ATA, PA	Y	Op	Small bowel	Alive
[25]	50	F	Unknown	OVAR	XR	BLE, EPEG, CDDP	ATA, AA, PA	Y	Op	Small bowel	Alive
[26]	53	F	13	Breast	CT	GEM, OX, Bevacizumab	AM, AA, BRM	Y	Op	Small bowel, multiple	Alive
[27]	58	M	14	Esoph	XR + CT	CAP, CDDP, TXT, Nivolumab	AM, AA, PA, BRM	Y	Op	Colon, multiple	Alive
[8]	58	F	15	Colon	CT	FOLFIRI, Aflibercept	AM, PA, BRM	Y	Op	Small bowel	Alive
[28]	58	M	18	NHL	XR + CT	MTX, Ara-C	AMs	N	Non	N/A	Alive
[29]	59	F	17	CERV	CT	CDDP, PTX, CBDCA, Bevacizumab	AA, PA, AA, BRM	Y	Op	Small bowel	Dead
[30]	60	M	5	NHL	XR	Rituximab	BRM	Y	Op	Small bowel	Dead
[24]	60	M	14	NHL	XR	CHOP	AA, ATA, PA	Y	Op	Stomach	Alive
[9]	60	M	16	Lung	CT	CBDCA, dFdCyd, PTX, Erlotinib	AA, AM, PA, BRM	Y	Op	Colon, multiple	Dead
[31]	61	M	Unknown	Lung	XR	CPT-11, CDDP, Nivolumab	PA, AA, BRM	Y	Non	N/A	Dead
[10]	63	M	1	RCC	XR + CT	Cabozantinib	BRM	N	Non	N/A	Alive
[32]	64	M	90	Lung	CT	CDDP, EPEG	AA, PA	Y	Op	Small bowel, colon	Dead
[33]	65	F	14	CML	XR + CT	COPADM	PA, ATA, AA, 3 AMs	Y	Non	N/A	Alive
[34]	66	F	30	Lung	CT	Gefitinib	BRM	Y	Non	N/A	Alive
[35]	66	F	30	OVAR	XR + CT	CBDCA, PTX	AA, PA	Y	Op	Colon	Alive
[36]	67	F	7	NHL	CT	CHOP	AA, ATA, PA	Y	Op	Stomach	Dead
[37]	72	M	7	Esoph	CT	CBDCA, PTX	AA, PA	N	Non	NA	Alive
[38]	74	F	14	Lung	XR + CT	Alectinib	BRM	Y	Non	NA	Alive
[39]	74	M	Unknown	Esoph	CT	CBDCA, PTX	AA, PA	N	Non	NA	Alive
[40]	75	M	1	Gastric	XR + CT	OX + 5-FU	AM, AA	Y	Non	NA	Dead
[41]	76	F	9	OVAR	CT	CBDCA, PTX	AA, PA	Y	Op	Colon	Alive
[9]	79	M	10	Lung	XR + CT	CBDCA, PTX, Erlotinib	AA, PA, BRM	Y	Op	Colon, multiple	Dead
[10]	81	M	1	RCC	XR + CT	Axitinib	BRM	Y	Op	None	Alive
[39]	83	M	Unknown	Lung	CT	Bevacizumab	BRM	N	Non	NA	Alive

5-FU, 5-fluorouracil; AA, alkylating agent; ALL, acute lymphocytic leukaemia; AM, antimetabolite; Ara-C, cytosine arabinoside; ATA, anti-tumour antibiotic; BLE, bleomycin; BRM, biological response modifier; CAP, capecitabine; CBDCA, carboplatin; CDDP, cisplatin; CERV, cervical cancer; CHEMO, chemotherapy; CHOP, cyclophosphamide, doxorubicin, vincristine, and prednisone; CML, chronic myeloid leukaemia; COPADM: cyclophosphamide, vincristine, prednisone, adriamycin, and methotrexate; CPT-11, irinotexan; CT, computed tomography; DRC, daunorubicin; EBV-LPD, Epstein-Barr virus lymphoproliferative disorder; EPEG, etoposide; Esoph, oesophageal; F, female; FOLFIRI, irinotecan, 5-fluorouracil, and leucovorin; FOLFOX, leucovorin, 5-fluorouracil, and oxaliplatin; GEM, gemcitabine hydrochloride; HL, Hodgkin's lymphoma; M, male; MTX, methotrexate; N, no; NA, not applicable; NHL, non-Hodgkin's lymphoma; Non, non-operative intervention; NP, natural product; Op, operative intervention; OVAR, ovarian cancer; OX, oxaliplatin; PA, plant alkaloid; PERF, perforation; PTLD, post-transplant lymphoproliferative disorder; PTX, paclitaxel; RCC, renal cell carcinoma; TXT, docetaxel; V, vincristine; VAD, vincristine, adriamycin, and doxorubicin; XR, X-ray; Y, yes.

patients were managed surgically (61.8%), and the patients who were managed operatively had a higher 30-day mortality rate than those who were managed non-operatively (33% vs. 23.1%, respectively). This increased rate could be partially attributed to the hostile operative field in the setting of recent chemotherapy, as previously discussed. This finding is in concordance with previous studies of emergency surgery for the management of perforated bowel malignancies, which reported mortality rates as high as 40% under these circumstances[54].

Table 3

Patients' characteristics and findings

	Adults ($n=26$)	Paediatric ($n=8$)	Total cases ($n=34$)
Median age	63.5	11.5	60
Sex, *n* (%)			
Male	15 (57.7)	6 (75)	21 (61.8)
Female	11 (42.3)	2 (25)	13 (38.2)
Presentation, *n* (%)			
Symptomatic	21 (80.8)	6 (75)	27 (79.4)
Asymptomatic	5 (19.2)	2 (25)	7 (20.6)
Malignancy, *n* (%)			
Solid organ	20 (76.9)	0	20 (58.8)
Haematological	6 (23.1)	8 (100)	14 (41.2)
Management strategy, *n* (%)			
Operative	15 (57.7)	6 (75)	21 (61.8)
Non-operative	11 (42.3)	2 (25)	13 (38.2)
Perforation site(s), *n* (%)			
Small bowel	5	—	5 (23.8)
Colon	3	—	3 (14.3)
Stomach	2	—	2 (9.5)
Appendix	—	1	1 (4.8)
Multiple sites	5	1	6 (28.6)
None	1	3	4 (18.9)
30-day mortality	34.6%	12.5%	29.4%

Several factors typically go into deciding the optimum management strategy for a patient presenting with pneumoperitoneum. These include the patient's hemodynamic status, frailty, and overall prognosis. Common non-operative therapeutic techniques include the use of broad-spectrum intravenous antibiotics, bowel rest, intravenous fluid resuscitation, and serial abdominal exams. Our scoping review showed that of patients presenting with pneumoperitoneum secondary to chemotherapy, 38.2% were managed non-operatively and had a lower 30-day mortality than the operative group. In the non-cancer patient population, non-operative management is typically reserved for hemodynamically stable patients with small, contained perforations[55,56]. Extrapolating this to our study, 7 of the 13 patients managed non-operatively were noted to be asymptomatic and hemodynamically stable, with pneumoperitoneum that was either found incidentally on routine imaging or during work-up for other etiologies. Of note, 3 of the 11 adult patients in the non-operative cohort were transitioned to comfort measures, given their overall poor prognosis.

Our study also found that 3 adult patients presented with abdominal symptoms and were managed non-operatively with bowel rest, intravenous antibiotics, and close monitoring with noted improvement in their abdominal pain. Prior to initiation of feeding, one patient had a water-soluble contrast study performed confirming no active extravasation in the gastrointestinal tract[38,] and one patient had a repeat X-ray showing resolution of pneumoperitoneum[33]. For the last patient in this cohort, the decision to start enteral feeds was based purely on clinical progress, and a repeat CT scan prior to discharge showed a resolution of pneumoperitoneum[34]. All three of these patients were alive at 30 days post-presentation.

One explanation for the lower 30-day mortality rate in the non-operative cohort could be that many of these patients were more clinically stable upon presentation than the operative cohort and, therefore, less likely to experience the morbidity and mortality associated with pneumoperitoneum. Indeed, more than half of these patients (53.8%) did not even have any abdominal symptoms upon presentation. However, our data do show that in at least 3 of the 11 adult patients (27.3%), the constellation of symptoms and clinical picture had a bleak prognosis, and they died shortly after comfort measures were initiated. As such, the decision-making process for patients who are hemodynamically unstable should include a careful evaluation of the goals of care, taking into account the patient's comorbidities, overall prognosis, and the anticipated quality of life. Our study also highlights the need for more studies on patients with a history of recent chemotherapy who require emergent surgical operations in situations where there is clinical equipoise. Patients with a relatively common abdominal malignancy, such as colon or rectal cancer, who have recently received chemotherapy would make the ideal pool to investigate by looking at various national databases.

In addition, while our study showed that mortality was higher in the operative group compared to the non-operative group, surgeon decision-making—who to operate on and when—was not able to be elucidated in this retrospective review. It is very likely that surgeons clinical judgement, from years of experience, informed their selection of which patients were likely to do well operatively versus non-operatively. There is, therefore, an opportunity for prospective studies that take into account surgeon decision-making in such cases where there is clinical equipoise on the optimal management strategy for patients with recent chemotherapy who require an emergent general surgery operation.

One of the limitations of this study is that it only includes articles published over a 33-year period (1990–2022). Although it excludes articles published earlier than 1990, this period was chosen to capture more recent trends in the management of this patient population and thus aid in the formulation of current and practical patient management guidelines. Given the scarcity of published literature on the subject, the sample size of the study is relatively small. As most of the patients were treated with multiple chemotherapeutic agents, it was not possible to pinpoint a single drug as the causative agent. In addition, it was not possible to stratify patients based on perioperative risks as this information was not available in the case reports. Lastly, due to the nature of this study as a scoping review, our findings are broad, and additional studies are warranted to synthesize and draw more specific conclusions. Despite these limitations, our findings strongly suggest pursuing non-operative management in this patient population whenever possible.

Conclusions

Chemotherapy-associated bowel perforation in patients actively undergoing chemotherapy is a rare yet highly morbid condition, with an overall mortality of ~30%, regardless of the choice of management strategy. Although the operative morbidity of emergency general surgery in cancer patients is known to be higher than in the non-cancer population, our study uniquely shows that operative intervention carries an overall higher mortality rate than non-operative intervention in this patient population. Additionally, we found that in patients who have abdominal pain but are hemodynamically stable and non-toxic, non-operative management with bowel rest, broad-spectrum

antibiotics, close monitoring, and repeat imaging prior to initiation of enteral feeds is the preferred option that avoids the morbidity and mortality of surgical exploration. We thus recommend that clinical presentation and oncological prognosis should both be carefully considered prior to deciding to surgically explore patients presenting with pneumoperitoneum who are actively undergoing chemotherapy. Early goals of care should be determined by patients and their families, and the risks, morbidity, and mortality of operative intervention should be thoroughly discussed.

Ethical approval

Ethical approval is not required for the publication of scoping reviews at the University of Tennessee Health Science Center in Memphis.

Consent

As this is an analysis of secondary data, no informed consent was required.

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Author contribution

Study conception and design: R.M.M. and D.A.F.; Data acquisition and curation: R.M.M., C.R., J.K., C.A. and H.M.J.; Data analysis: R.M.M., C.S.M., N.N.Z., J.L.A., M.B.O., J.S.N., D.A.F.; Writing original draft: R.M.M., H.M.J.; Critical revisions and edits: R.M.M., N.N.Z., J.L.A., M.B.O., J.S.N., C.S.M., D.A.F.; Overall supervision, D.A.F. All authors approved the final manuscript.

Conflicts of interest disclosure

The authors report no proprietary or commercial interest in any product mentioned or concept discussed in this article.

Research registration unique identifying number (UIN)

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2. Unique Identifying number or registration ID: none.
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Guarantor

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