# Gastrointestinal emergencies in critically ill cancer patients

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## ARTICLE INFO

## ABSTRACT

*Purpose:* To describe gastrointestinal emergencies in cancer patients.

*Methods:* All cancer patients admitted to the medical ICU of Saint-Louis Hospital for an acute abdominal syndrome during the study period (1997–2011) were included.

*Results:* A total of 164 patients were included. The most common diagnoses were: neutropenic enterocolitis (NE) (n = 54, 33%), infectious colitis and peritonitis (n = 51, 31%), bowel infiltration by malignancy (n = 14, 9%), and mucosal toxicity of chemotherapy (n = 12, 7%). Microbiologically documented infections were reported in 82 patients (50%), including 12 fungal infections. Twenty-seven patients (16%) underwent urgent surgery. The hospital mortality rate was 35%. Five factors were independently associated with hospital mortality: the Simplified Acute Physiology Score II (SAPS II) score on day 1 (OR 1.03/SAPS II point, 95% CI 1.01 to 1.05), microbiological documentation (OR 0.27, 95% CI 0.11 to 0.64), neutropenia (OR 0.42, 95% CI 0.19 to 0.95), allogenic hematopoietic stem-cell transplantation (HSCT) (OR 5.13, 95% CI 1.71 to 15.4), and mechanical ventilation (OR 3.42, 95% CI 1.37 to 8.51).

*Conclusions:* Gastrointestinal emergencies in cancer patients are associated with significant mortality. Mortality correlated both with the severity of organ failure upon ICU admission and the underlying diagnosis. Interestingly, patients admitted to the ICU with neutropenia had better survival.

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## 1. Introduction

Cancer is a leading cause of death worldwide [1,2]. In recent decades, cancer patients have benefited from significant diagnostic and therapeutic advances which offer extended survival [3,4]. As a consequence, a growing number of people are living with solid tumors or hematological malignancies [5]. These patients are at high risk for life-threatening complications related to the malignancy itself or the side-effects of its treatment.

The intestinal tract is a common site for various infectious and non-infectious complications. Chemotherapy-related mucositis and neutropenia put these patients at risk of infections of abdominal origin and subsequent severe sepsis or septic shock [6-9]. Several entities are recognized, including neutropenic enterocolitis (NE), *Clostridium difficile* colitis, cholecystitis, cholangitis, appendicitis, and *Cytomegalovirus* colitis [10,11]. Among the non-infectious diseases, bowel obstruction, gastrointestinal hemorrhage, hypovolemia related to chemotherapy-induced vomiting and diarrhea, and bowel graft-versus-host disease (GVHD) in allogeneic hematopoietic stem cell transplant (HSCT) recipients have been reported [12,13]. These complications could be challenging to diagnose and to treat. Indeed, clinical signs and symptoms are not pathognomonic of any single entity and might be diminished in immunocompromised hosts. A combination of clinical features, abdominal imaging, microbiologic, and sometimes histopathological data is often required to make the final diagnosis. In addition, the appropriate use of surgery in the management of these patients remains a matter of debate [14-16].

Very few studies have evaluated abdominal complications of cancer patients in the ICU setting. The objectives of this study were to describe the clinical features and outcomes of gastrointestinal emergencies in

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this population. In addition, we aimed to identify factors associated with hospital mortality.

## 2. Methods

This study was approved by our institutional review board (CECIC Clermont Ferrand – IRB no.5891; Ref: 2007-16). According to the French law, informed consent was not required in this retrospective observational study with anonymous data collection.

### 2.1. Design and setting

We retrospectively included consecutive adult patients with cancer admitted to the medical ICU of Saint-Louis University Hospital for an acute abdominal syndrome associated with at least 1 organ dysfunction, between January 1, 1997 and July 31, 2011.

The Saint-Louis University Hospital is a 650-bed public hospital, with 330 beds dedicated to patients with various conditions associated with immunodeficiency (hematological malignancies, solid cancers and solid organ transplantation). There are seven hematology wards (adolescent and young adult hematology, acute leukemia, senior hematology, clinical immunology, myeloma, lymphoma, and allogeneic stem cell transplantation) and four oncology wards (general oncology, lung cancer, gastrointestinal oncology, and radiation therapy).

The medical ICU of Saint-Louis Hospital is a 12-bed unit which admits 750–850 patients per year, of whom about one-third have hematological malignancies. Information on the organization of the ICU and criteria for ICU admission have been published elsewhere [17]. Mandatory ICU admission reasons are defined by at least 1 organ failure and the need for at least 1 of the following therapies: supplemental nasal oxygen ≥3 L/min, use of vasoactive drugs, sustained volemic expansion, invasive or non-invasive mechanical ventilation, or renal replacement therapy. At our institution, intensivists, hematologists, and digestive surgeons are available 24 h a day, seven days a week and work together to manage all high-risk cancer patients.

### 2.2. Eligibility criteria

Patients were identified through the database of the ICU department. All cancer patients admitted to the ICU during the study period for gastrointestinal emergencies defined by the association of abdominal symptoms (severe abdominal pain, distension or cramping, gastrointestinal bleeding, severe diarrhea, or bowel obstruction) with at least 1 organ dysfunction (shock, acute kidney injury, acute respiratory failure or neurological disorders) were included.

### 2.3. Data collection

All data were obtained from medical records and patient charts. Baseline patient characteristics were collected, including demographics, comorbidities, underlying disease, and Performance Status (PS) within three months before ICU admission. Data regarding the type of cancer, cancer status, and anticancer treatments were abstracted from the medical charts. Variables recorded regarding ICU admission and treatments were: data relative to clinical presentation, reason for ICU admission, time of admission and discharge from ICU, diagnosis, therapies implemented, microbiological documentation whenever possible, and ICU outcome data. Disease severity at ICU admission was assessed using the Simplified Acute Physiology Score II (SAPS II) score and the Logistic Organ Dysfunction System (LODS) at day 1 [18,19].

The gastrointestinal complications encountered were classified as one of the following well-recognized syndromes: neutropenic enterocolitis (NE), infectious colitis or peritonitis, intestinal infiltration by malignancy, acute intestinal ischemia, chemotherapy-induced toxicity, graft versus host disease (GvHD), others (cholecystitis, cholangitis, diverticulitis, and appendicitis), and unknown. For the diagnosis of neutropenic enterocolitis, at least 2 of the 3 major criteria (including neutropenia which was a mandatory criteria) and 2 of the 5 minor criteria proposed by Gorschlüter had to be present in addition with the exclusion of *Clostridium difficile* colitis and GvHD [11,20]. Radiographic findings (including ultrasonography and computerized tomography (CT) scanning of the abdomen and/or pelvis), gastrointestinal (GI) endoscopy features, and surgical interventions were also reported. The clinical, laboratory, imaging data, endoscopic and surgical reports in each patient were reviewed by DL and EC who reached a consensus regarding the final diagnosis. Vital status at hospital discharge was available for all patients.

The primary outcome was the percentage of patients who were alive at hospital discharge. The main study objective was to identify prognostic factors associated with this outcome.

### 2.4. Statistical analysis

Quantitative variables are described as the median (interquartile range, IQR) and compared using Wilcoxon's rank sum test; qualitative variables are shown as counts (percent) and compared using Fisher's exact test. Hospital mortality was analyzed as a binary variable. Univariate analysis was performed using the abovementioned tests and predictors that were significant at a 10% level in the univariate analysis were considered for the multivariate analysis. The multivariate model selected was a logistic regression model using a backward stepwise selection method, based on the *p*-values (threshold = 0.05). The selected model was further validated by bootstrapping [21]. The log-linearity of the quantitative variables was checked. A test of goodness of fit was performed using le Cessie-van Houwelingen's method [22]. The measures of association between mortality and the variables are presented, with odds ratios and confidence intervals at 95%.

All tests were two-sided and *p*-values lower than 5% were considered to indicate significant associations. Analyses were performed using the R statistical platform, version 3.2.2.

## 3. Results

### 3.1. Study population

Among the 3222 cancer patients admitted to the ICU during the study period, 171 (5.3%) were admitted with acute abdominal symptoms. We report on the 164 patients with no missing data (Fig. 1). Patient characteristics are reported in Table 1. Of the 164 patients, 130 (79%) had hematological malignancies and 34 (21%) solid cancer. The median time between malignancy diagnosis and ICU admission was 5.3 (interquartile range, 1.4–23) months. Most patients (*n* = 111, 79%) had received chemotherapy within 30 days before ICU admission. Bone marrow or hematopoietic stem-cell transplantation (BMT/HSCT) had been performed in 43 patients (26%); the transplantations were autologous in 20 patients and allogeneic in 23 patients. Neutropenia was present upon ICU admission in 76 patients (47%), among which 50 (65.8%) witnessed neutropenia recovery throughout the ICU stay. Cancer status upon ICU admission was newly diagnosed or undergoing first-line chemotherapy in 87 (53%) patients, and 122 (75%) had a good general condition (Performance Status 0–1).

### 3.2. Characteristics of abdominal diseases

Abdominal symptoms started 1 (0–5) day before ICU admission. Clinical findings commonly encountered were abdominal pain (*n* = 111, 68%), diarrhea (*n* = 99, 60%), and abdominal distention (*n* = 70, 43%). GI bleeding was reported in 39 patients (24%) and bowel obstruction in 28 (17%) patients. Four abdominal syndromes accounted for 80% of cases: NE (*n* = 54, 33%), infectious colitis and peritonitis (*n* = 51, 31%), bowel infiltration by malignancy (*n* = 14, 9%), and mucosal toxicity of chemotherapy (*n* = 12, 7%) (Table 2). Microbiologically