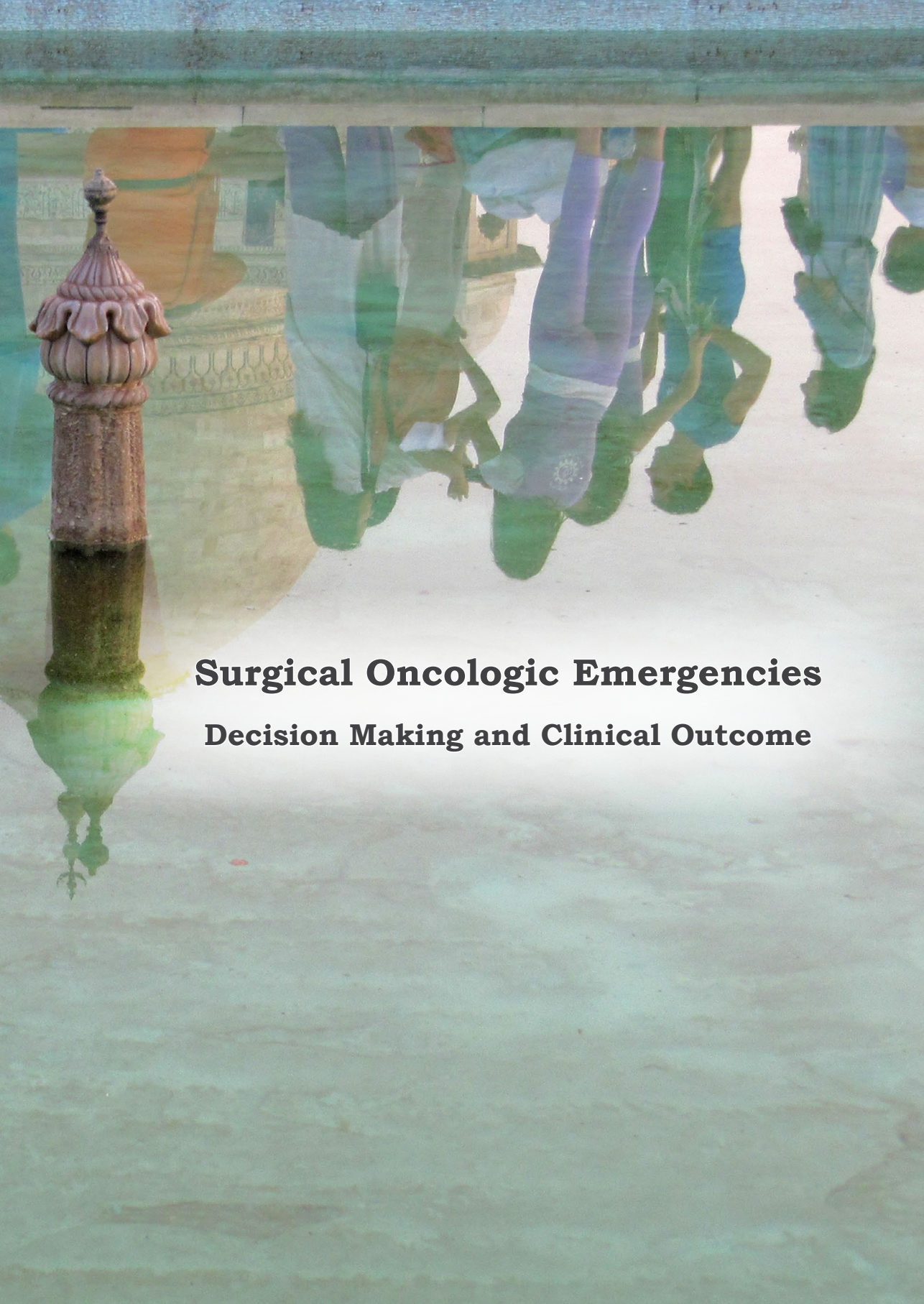

Surgical Oncologic Emergencies

Decision Making and Clinical Outcome

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Decision Making and Clinical Outcome

M.R.F. Bosscher

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Prof. dr. G.M. van Dam

Reflection

Each time I see the Upside-Down Man
Standing in the water,
I look at him and start to laugh,
Although I shouldn't oughtter.
For maybe in another world
Another time
Another Town,
Maybe HE is right side up
And I am upside down

From: *A light in the Attic* by Shel Silverstein, 1981

Paranimfen

Sabine Bakhuizen

Annemieke Coester

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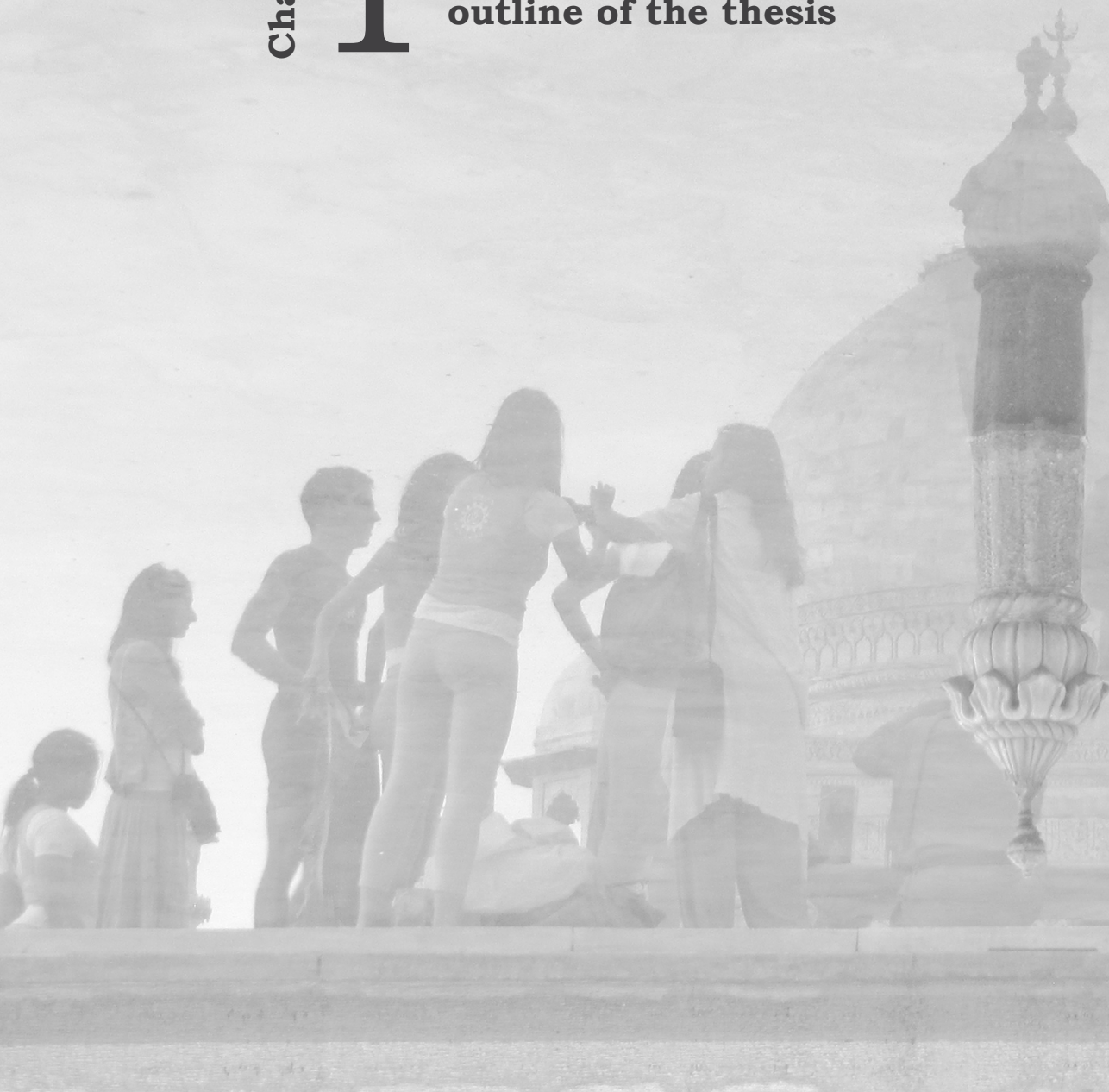
Chapter 1

General introduction and outline of the thesis



Cancer incidence and prevalence

The incidence of all types of cancer in the Netherlands in 2013 was 101,214 [1]. Due to the continuing growth and aging of the population, the incidence of cancer is expected to increase with approximately 3% per year in the upcoming years [1-3]. Due to early detection and improved cancer treatment, the prevalence of cancer will increase even more; a higher number of patients will be cured, and the number of patient alive with disease will also increase. The exposure of patients with (a history of) cancer to any physician, electively or non-electively, will rise accordingly.

Surgical oncologic emergencies

An oncologic emergency is defined as an acute, potentially life threatening condition that has developed directly, or indirectly, as a result of malignant disease or cancer treatment [4,5]. The majority of these conditions require non-elective treatment. Sometimes, emergency surgical procedures may be necessary as a remedy or temporary relief.

Cancer patients can experience oncologic emergencies of various severities and at all stages of disease. In general medical practice, there are many medical guidelines and protocols regarding emergency care, and all medical professionals receive training in the management of emergency situations within their specialty. Nevertheless, there is a serious lack of guidelines regarding the management of oncologic emergencies. The management of these oncologic emergencies often depends on the personal decisions of the physician who is confronted with these emergencies. Initial treatment decisions can have great impact on the final outcome, but emergency physicians are generally not trained in complex cancer care.

The heterogeneity of the common cancer population and the variety of oncologic emergencies complicate the process of decision making in clinical practice. In emergency situations, which often occur outside office hours, there is usually shortage of time, resources, and (trained) personnel.

Decisional difficulties and mortality

Certain oncologic emergencies can be signs of advanced, end-stage disease. In previous studies, mortality rates between 1% and almost 67% have been reported after visits of cancer patients to the emergency room [6]. Patients who are at the end of life often will not benefit from invasive treatment, and many interventions can even have a negative impact on the remaining life-span and the quality of life [7]. It is important that (emergency) physicians who are confronted with oncologic emergencies, take into account the remaining life expectancy when they decide on the extend of treatment for patients with oncologic emergencies [8]. The awareness regarding the occurrence and consequences of oncologic emergencies should be increased. Physicians need to differentiate between patients with a fair prognosis and patients who face the end of their lives. In this way, the most suitable treatment for each individual patient can be instigated, e.g. 'personalized emergency cancer care'.

It is against the nature of medical professionals to abstain from treating a patient. In accordance with the Hippocratic Oath, physicians feel the duty for *healing those who seek [my] help*. The modern English version of the Hippocratic Oath however, contains several phrases which are even more important in medical practice [9];

I will apply, for the benefit of the sick, all measures [that] are required, avoiding those twin traps of overtreatment and therapeutic nihilism.

I will remember that there is art to medicine as well as science, and that warmth, sympathy, and understanding may outweigh the surgeon's knife or the chemist's drug.

And

I will not be ashamed to say "I know not," nor will I fail to call in my colleagues when the skills of another are needed for a patient's recovery.

These phrases apply to the principle of the universally known Latin expression *Primum non nocere*, which is often thought to originate from Hippocrates but was merely introduced in a book published as late as 1860 [10]. Regarding any patient in medical practice, physicians

should keep in mind that every medical treatment will have its consequences. Some of these consequences may be more severe or longer lasting than those of other treatment options. “Overtreatment” means that there is lack of benefit, and it can even cause serious harm. One must not forget that a surgeon’s knife will always result in a wound that requires healing. Surgery, or other invasive interventions, should only be performed when the outcome is expected to be advantageous for the patient.

According to a report evaluating provided healthcare in the last phase of life, which was recently published (March 5, 2015) by the Royal Dutch Medical Association (KNMG), the three most common forms of overtreatment experienced by patients were too many and/or invasive diagnostic interventions (15%), hospital visits for admission or treatment (14%), and surgery (14%) [11]. Defective communication with the patient or other care givers, not listening to the patient’s preferences, too much handling according to general protocols, and the lack of adjusting standard treatment to the situation of the individual patient were regarded as the most important causes for overtreatment.

In 1982, the Confidential Enquiry into Perioperative Deaths (CEPOD) was initiated in the United Kingdom [12]. It was a joint venture between surgical and anesthetic specialists, and aimed to assess through a peer review process the quality of surgical and anesthetic practice by evaluating cases of patients with perioperative mortality. The cases that were evaluated for this report included a wide range of surgical procedures of various surgical subspecialties [13]. After evaluation of 2391 cases of patients who died within 30 days after a surgical procedure, one of the recommendations in their report of 1987 was:

The decision not to operate is difficult. Humanity suggests that patients who are terminally ill or moribund should not have operations (i.e. non life saving), but should be allowed to die in peace with dignity.

In the next years, similar recommendations were made in subsequent reports of the nationwide successor of CEPOD, the National Confidential Enquiry into Perioperative Deaths (NCEPOD). The main recommendation in the report of 1996/1997 was [14]:

It is a surgical skill to recognize when surgery will be too adventurous, ill advised or futile,

given the condition of the patient. It is difficult to resist pressure to operate, whether this comes from the patient, relatives or medical colleagues but it must be recognized that surgery cannot solve every problem.

They also recommended specifically on decisions regarding surgical treatment for advanced cancer patients:

Patients and their relatives need to recognize the limits of surgery in advanced malignant disease. A decision to operate may not be in the best interests of the patient.

Multidisciplinary cancer care

The Calman-Hine report, published in 1995, identified apparent variation in recorded outcomes of treatment for cancer within the United Kingdom [15]. In this report, the development of multiple levels of care with specialized cancer units and centers including multidisciplinary management for all cancer patients was recommended by the authors. In this way, all cancer patients would have access to a uniformly high standard of care. They highlighted the importance of effective communication and clear information for care givers, patients and families. In the past decade, healthcare professionals and many international (health) organizations have expressed their support for multidisciplinary teams, and multidisciplinary management has been implemented in general cancer care [16,17].

The organization of cancer care nowadays, including multidisciplinary cancer conferences (MCC's), is designed for patients electively referred. Since specialized cancer care is normally only available during office hours, it is not adequately designed to serve those cancer patients who are admitted as emergencies. Non-elective treatment decisions are still often made without multidisciplinary evaluation, with great gaps in the available information and without the right expertise [7]. As decisions regarding treatment for patients with surgical oncologic emergencies are often complex, and these patients especially would benefit the most from multidisciplinary management, the absence of it outside of office hours is a serious problem. According to the NCEPOD report of 2001, almost two-third of

512 cancer patients with perioperative mortality (<30 days) were admitted either urgently or as an emergency, and only a minority of these patients was discussed in an MCC [18]. For the patients of whom the intention of the surgical procedure was documented, most patients with perioperative mortality underwent surgery with palliative intent (43.8%), diagnostic intent (9.5%), or the intention was documented as "not sure" (8.0%). This illustrated the uncertainty and incompleteness of information, even after the initiation of invasive treatment.

Acute oncology pathways

For various medical conditions, specialized care pathways with multidisciplinary dedicated teams have been developed to improve the efficiency and quality of medical care [19]. To facilitate optimal care for cancer patients who require non-elective treatment, the implementation of specialized acute oncology pathways could result in improved coordination of personalized care in acute situations. Standard specialized multidisciplinary care can help to restrict unnecessary invasive or costly procedures. When decisions to refrain from invasive treatment are made, end of life care can be decided on and provided more efficiently, and the length of hospital stay can be reduced to a minimum. Few studies have proposed and evaluated the implementation of such pathways with favorable outcome [20-25]. Unfortunately, this form of specialized emergency cancer care has not (yet) been integrated in standard medical practice.

Outline of this thesis

To achieve consensus that emergency cancer care requires substantial changes, it is important to create awareness of the rate of occurrence of surgical oncologic emergencies, and of the management and outcome in current practice.

In *Part I - Definition and occurrence of surgical oncologic emergencies*, surgical oncologic emergencies are defined, and a summary is given of potential surgical oncologic

emergencies, including their approaches. Subsequently, reasons for presentation of cancer patients at the emergency room for surgical oncologic consultation with the subsequent mortality are explored.

In *Part II – Current management and clinical outcome of surgical oncologic emergencies*, the costs of current hospital care for patients with surgical oncologic emergencies and the current rate of multidisciplinary management are evaluated.

In *Part III – Survival prediction*, factors associated with mortality after surgical oncologic emergencies are investigated, in order to improve better insight into the clinical outcome and to rather recognize patients who are at the end of life.

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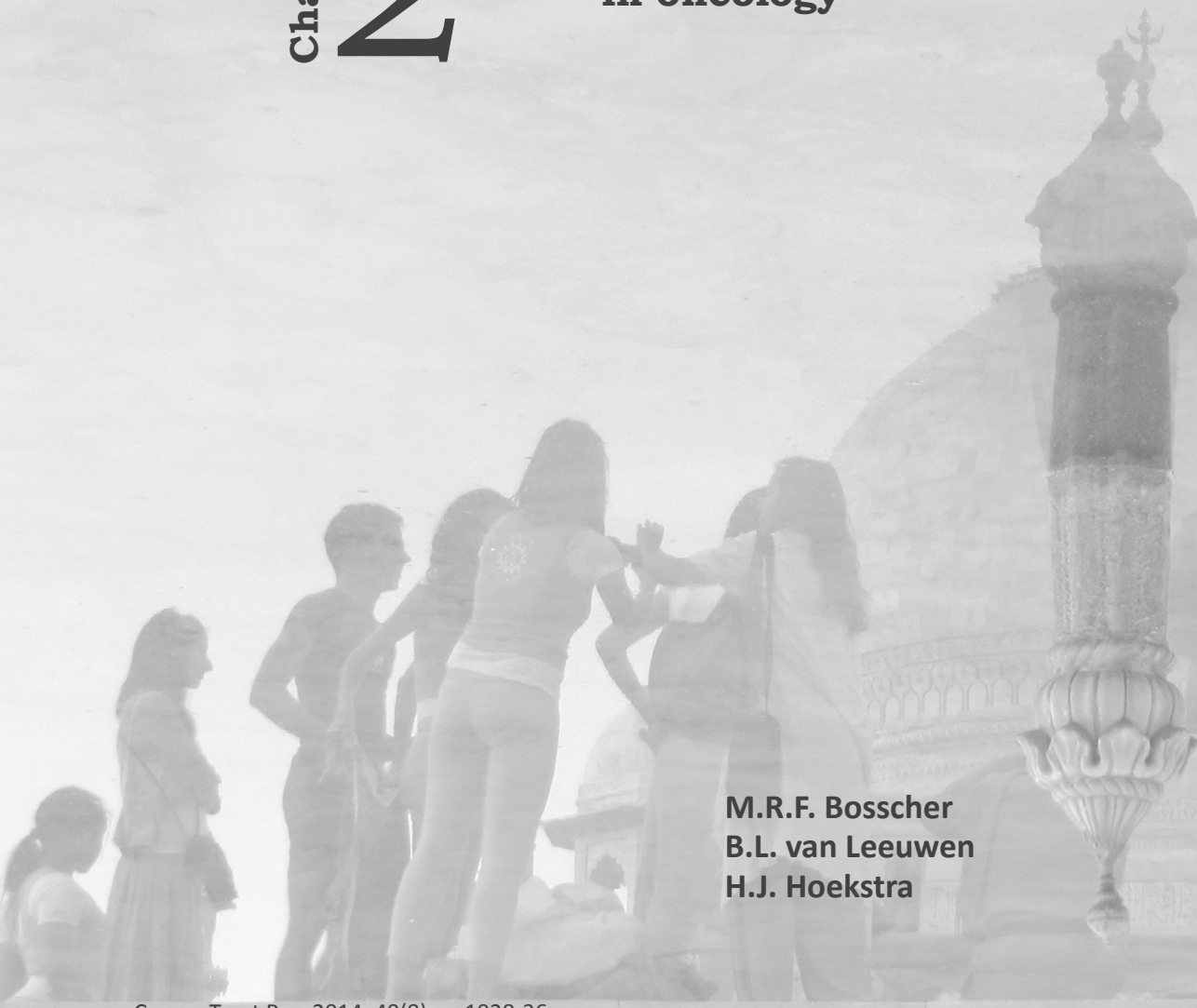
Part I
Definition and occurance of surgical oncologic emergencies

Chapter 2

Surgical emergencies in oncology



M.R.F. Bosscher
B.L. van Leeuwen
H.J. Hoekstra

Cancer Treat Rev. 2014. 40(8): p. 1028-36

Abstract

An oncologic emergency is defined as an acute, potentially life threatening condition in a cancer patient that has developed as a result of the malignant disease or its treatment. Many oncologic emergencies are signs of advanced, end-stage malignant disease. Oncologic emergencies can be divided into medical or surgical. The literature was reviewed to construct a summary of potential surgical emergencies in oncology that any surgeon can be confronted with in daily practice, and to offer insight into the current approach for these wide ranged emergencies.

Cancer patients can experience symptoms of obstruction of different structures and various causes. Obstruction of the gastrointestinal tract is the most frequent condition seen in surgical practice. Further surgical emergencies include infections due to immune deficiency, perforation of the gastrointestinal tract, bleeding events, and pathological fractures.

For the institution of appropriate treatment of any emergency, it is important to determine the underlying cause, since emergencies can be either benign or malignant of origin. Some emergencies are well managed with conservative or non-invasive treatment, whereas others require emergency surgery. The patient's performance status, cancer stage and prognosis, type and severity of the emergency, and the patient's wishes regarding invasiveness of treatment are essential during the decision making process for optimal management.

Introduction

Over the past decades, there has been an increasing incidence of cancer diagnoses, resulting from changing lifestyles, ageing of the population and the implementation of screening programs [1-3]. Luckily survival has improved due to earlier detection and the development of more efficient cancer specific treatment regimens. Consequently, there will be an increasing number of patients with a history of cancer presenting at the Emergency Room (ER). Cancer patients can present at the ER for various reasons; symptoms caused by malignant disease, complications of cancer treatment, or symptoms not directly related to malignant disease or treatment [4-9]. As cancer patients admitted through the ER often have advanced disease, and the frequency of visits to the ER rises near the end of life, this patient category requires special attention [10,11].

An oncologic emergency is defined as an acute, potentially life threatening condition in a cancer patient that has developed, directly or indirectly, as a result of the malignant disease or cancer treatment [12,13]. Any cancer patient can experience emergencies that require surgical consultation and possible surgical treatment, and any physician can be confronted with these emergencies. Therefore, an understanding of the pathophysiology and prognosis of the various emergencies is necessary for correct management. Many emergencies in oncology are signs of advanced, end-stage disease. To determine which procedures should be undertaken or avoided, it is essential that a surgeon is informed on the performance status of the individual patient, the cancer stage and prognosis, (need for) future cancer-treatment, and the patient's wishes regarding aggressive interventions and treatment at the end of life [14-17].

In the past, several reviews have been published concerning emergencies in oncology and their management in general [5,12,13,18-24]. These oncologic emergencies are mostly categorized as metabolic, hematologic, cardiovascular, infectious, and structural [5,12,21,24]. These emergencies can also be categorized as medical or surgical [15]. However, to our knowledge, no review article has been written on the surgical emergencies in oncology specifically. For this article, the literature was reviewed to construct a summary for potential surgical emergencies in oncology that any surgeon can be confronted with in daily practice, and to offer insight into the current approaches for these wide ranged emergencies. Guidelines for

management are given, but for some cases no details of specific procedures are described, since institutions might have different protocols for execution and management.

Obstruction

Cancer patients can experience symptoms of obstruction of different structures and various causes [15]. A substantial number of obstructions is benign in nature and not caused by tumor mass [15,25].

Obstruction of the gastrointestinal tract

Obstruction of the gastrointestinal tract is the most frequent emergency seen in surgical practice and is characterized by clinical intolerance to oral intake resulting in nausea, vomiting, (abdominal) pain, and absence of stool passage [26-29]. Many patients do not experience a solitary obstruction, but concurrent intestinal obstructions [28].

Initial treatment of any obstruction in the gastrointestinal tract starts with conservative treatment; i.e. restoration of fluid and electrolyte balance, alternatives for feeding, restriction of medications that have a paralytic effect on the intestines, and nasogastric tube placement for decompression with stimulation of intestinal passage with laxatives for distal obstructions [15]. This conservative regimen will keep the patient in (the most) optimal condition and it gains time for diagnostic methods in order to identify the origin of the obstruction, staging of the malignant disease, and multidisciplinary evaluation. Minimally invasive diagnostic methods include imaging studies, endoscopy, and laboratory tests including tumor markers. The route for nutrition depends on the site of obstruction and the patient's clinical tolerance for oral intake. Options for feeding are liquid dietary supplements, a feeding tube past the obstruction if possible, or total parenteral nutrition. Nutrition for patients with obstruction of the small or large intestine should be given through the parenteral route, as a feeding tube functions poorly in case of obstruction

more distally. A conservative treatment should be instituted during the diagnostic process for as long as the cause of obstruction is unknown or to see if the obstruction resolves spontaneously, but not longer than 3-7 days [15,30-32]. After this period, decisions have to be made regarding invasive therapy, (diagnostic) surgery, or refraining from any intervention and withdrawel of care. It is important that these decisions are made multidisciplinary and in deliberation with the patient and family; to provide the patient with the essential information regarding prognosis, treatment options and the expected impact, and to follow the patient's and families wishes [33,34]. The routine use of long term parenteral nutrition for patients with malignant obstruction is controversial and should be reserved for patients with minimal tumor burden who will receive surgery or chemotherapy in the near future [34]. When refraining from interventions, it must be considered that continuation of nutrition for the terminally ill patients doesn't influence survival, and may even reduce quality of life by the presence of feeding tubes or indwelling catheters. Table 1 provides a summary of causes and treatment options for the variety of obstruction symptoms.

Causes

Proximal esophageal and gastric outlet obstruction can lead to the initial presentation of esophageal or gastric cancer, or be a symptom of recurrence of locally advanced disease [15,35-37]. It may be caused by intraluminal tumor presence, intraluminal invasion, or extrinsic compression by tumor mass. Benign causes of esophageal obstruction are treatment-related edema, initial worsening of obstructive symptoms due to chemo- or radiation therapy, and anastomotic strictures after surgery. With the exception of (postoperative) gastroparesis, gastric outlet obstruction is malignant in nature and usually a sign of advanced, incurable disease [38].

Patients with a history of cancer, frequently experience symptoms of small intestine obstruction [15,27]. Benign causes have been reported to account for about 18% up to 55% of cases of small intestine obstruction, including postoperative adhesions, intestinal strangulation or hernia, and structures following radiation therapy [27,32,39-41]. Malignant causes can be intraluminal tumor presence, intraluminal invasion, or extrinsic compression by tumor in primary disease, local recurrence, and peritoneal carcinomatosis [25,27,31,32,42]. Small intestinal obstruction due to recurrent cancer is commonly seen in colorectal cancer, ovarian cancer, gastric cancer and melanoma, and is often a sign of end-stage disease [12,31,42].

The time of the occurrence of obstruction symptoms after surgery tends to be shorter for malignant causes (within three years after the initial surgery), compared to benign causes (median time five years) [25,27,43]. Incomplete obstruction, non-permanent pain, the presence of ascites and a known cancer recurrence prior to the obstruction seem to be indicative for malignant small intestinal obstruction [25,27].

For patients with colorectal obstruction 80% of cases is malignant, and 10-30% of patients with colorectal cancer present with symptoms of obstruction [44]. Malignant colorectal obstruction is often caused by intraluminal tumor presence in cases of colorectal cancer, with the majority located in the left side of the colon [45,46]. Other malignant causes can be metastatic disease of other origin, and pelvic tumors causing obstruction through extrinsic colorectal compression or invasion [45,47]. A pseudo-obstruction, Ogilvie's syndrome, may mimic a mechanical obstruction [15,45,48]. Other forms of benign colorectal obstruction can be volvulus, diverticulitis, intussusception, and anastomotic strictures developed after surgery [45]. Colorectal obstruction becomes life-threatening when the presence of a competent ileocoecal valve leads to a closed-loop situation with distention of the colon and subsequent risk of colonic perforation [4,15,46].

Management

For proximal obstructions in locally advanced esophageal cancer, there is no indication for palliative surgical resection or bypass [15]. In contrast, some patients with gastric outlet obstruction and a good performance status, may benefit from surgery, e.g. bypass gastrojejunostomy, or distal gastrectomy [15,38,49,50]. Less invasive interventions to establish nutrition in patients with proximal obstruction and poor performance status are endoscopic stent placement, percutaneous gastrostomy or surgical jejunostomy for feeding past the obstruction, [15,35,36,51-55]. Esophageal stent placement and percutaneous gastrostomy should be reserved for patients with fair prognosis, e.g. benign strictures or patients who receive treatment with curative intent, since it is associated with a high complication rate [56-58]. For gastric outlet obstruction, surgery has the potential of causing less long term morbidity dependant on the life expectancy of the patient, by reducing the risk of re-obstruction compared to stent placement. Surgery may be considered for patients with a short tumor length, a single site obstruction, and a life expectancy greater than 60 days [34,59]. Endoscopic ablative techniques are available to reduce proximal obstruction; however, these techniques

have a substantial risk of bleeding or perforation and decreased peristaltic motility [36,60,61].

Conservative treatment with stimulation of intestinal passage appears ineffective in many cases of (benign and malignant) obstruction of the small intestine, as the obstruction symptoms often reoccur in 47% up to 72% of patients within one year after initial relief [30,31]. When the cause of the obstruction is benign, one should not hesitate to perform a laparotomy for adhesiolysis or bowel resection [25,27,31,42]. In the case of radiation enteritis, it is important to resect the entire diseased bowel segment to reduce recurrence, postoperative complications and mortality [62-66]. In cases of malignant origin, surgical interventions such as bowel resection, bypass, or ileostomy, may seem to provide in good palliation by reduction of symptoms and obstruction recurrence in progressive disease, but depend on the extend of disease in the individual patient [15,27,32,42]. The invasiveness of surgery is associated with high treatment related morbidity and mortality rates. Thus, in case of malignant obstruction, surgery for malignant obstruction should be reserved for patients with resectable disease, good performance status (ECOG≤1), and a life expectancy of more than 6 months [26,34,50]. Surgery for patients with peritoneal carcinomatosis is associated with a 30-day mortality of 21-40% and high recurrence rates [59]. Non-invasive treatment with palliation of discomfort remains the best treatment for patients with incurable disease with peritoneal metastases, and for those who are not fit for surgery [25,31,32,42]. The acrimonious aspect of obstructions of the small intestine is that in many cases, the origin of the obstruction is only identified by surgical exploration and/or the final pathology report.

The treatment of colorectal obstruction depends on the cause and the clinical severity of the presentation. Benign causes with presence or risk of ischemia, perforation, or volvulus require emergency surgery [45]. For less emergent presentations, endoscopic detorsion or stenting must be considered as alternatives for surgery.

In cases of malignant colorectal obstruction, the urgency of treatment depends on the risk of perforation and subsequent complications [67]. For relief of the obstruction, the most optimal treatment would be surgical resection, bypass, or ileo-/colostomy with or without subsequent staged resection [26,45,47,67,68]. Surgery is reported to be successful for control of obstruction symptoms in 42 - 80% of procedures [69-71]. Surgical options for obstruction of malignant origin depend primarily on the location of the tumor, extend of the disease, and clinical performance status of the patient [46,72,73]. When determining the appropriate

surgical procedure for palliative cause, the risks and consequences of treatment-related complications and the burden of an ileo-/colostomy should be taken into account. The focus of surgery should be on the clinical outcome, i.e. short term relieve of the obstruction, long term reduction of morbidity and mortality and establishing optimal quality of life [26,47]. Presence of total obstruction or ascites seems to be associated with worse outcome and a reduced rate of palliation of symptoms after emergency surgery [69].

As the patient's condition is often very poor in the emergency setting, especially for patients with end-stage disease, emergency surgery is associated with a treatment related morbidity up to 61%, 30-day mortality of 9.8%, and overall mortality of 15-37% [45,69,74]. Endoscopic alternatives for surgery include tumor ablation and decompression by stent placement [45,46,75]. Endoscopic techniques are also associated with complications such as stent migration, stent stenosis, reocclusion, or bowel perforation with subsequent tumor spread [44,76,77]. When the patient's condition allows surgery, emergency surgery leads to better clinical relief for malignant colorectal obstruction compared to stent placement alone (98.84% clinical success vs. 78.05%, p=0.001), without significant differences in mortality and morbidity [44,76]. However, endoscopic stent placement does have the benefit of lower pain scores shortly after the procedure, shorter procedure time and hospital stay, and minimal blood loss. Endoscopic stent placement can serve as a bridge to surgery at later stage or as palliative therapy, when surgery in the acute setting is not expected to be beneficial for the patient [45,75-79]. Previous studies are inconclusive in the long term advantages of the systemic use of stent placement to create elective opportunities for surgical resection [74,76-81]. It seems to provide in an increased primary anastomosis and decreased permanent stoma rates for left-sided obstruction, but there is no effect on the occurrence of anastomotic leakage, morbidity, and overall survival.

For patients with inoperable bowel obstruction, poor performance status (ECOG>2) and short cancer-related life expectancy, refraining from invasive procedures and discharge from the hospital with palliation of nausea, vomiting and pain may be the best management at the end of life. The definition of a short life expectancy remains an ethical discussion point.

Obstruction of the biliary tract

Malignant obstruction of the biliary tract can be due to intraluminal tumor presence, local invasion of primary disease, or due to metastases of cancers of distant origin [15,82]. Biliary obstruction can result in secondary cholangitis [82]. Symptomatic cholangitis is characterized by jaundice, pruritus, fever, and abdominal pain and it can cause fibrosis, cirrhosis, and ultimately liver failure. Malignant biliary obstruction is most often caused by mass lesions due to either adenocarcinoma of the pancreatic head, periampullary neoplasms, intra- or extrahepatic cholangiocarcinoma, and metastatic lymphadenopathy in the hepatoduodenal ligament [82,83]. It can also be caused by strictures developed after radiation therapy or surgery. The overall prognosis of malignant biliary obstruction is poor; many patients who are symptomatic already have advanced disease and palliative treatment is often the only option [82,83]. Symptomatic hyperbilirubinemia, resulting in pruritus, cholangitis, or sepsis, are indications for emergency drainage [15,82]. In absence of cholangitis, immediate decompression is not necessary and there is time for staging and the evaluation of options for resection [15].

Management

Possible interventions for biliary obstruction are percutaneous transhepatic or endoscopic (external or internal) drainage of the biliary system, balloon dilatation, or stent placement [15,82,84]. Further alternatives are endoscopic sphincterotomy, and - the most invasive option - surgical biliary-enteric bypass [15,82,83]. As these procedures may lead to secondary infection and obstructive cholangitis, surgical treatment should only be performed in case of relatively fair oncological prognosis [15,83].

For patients with obstruction at the level of the common hepatic duct or higher, poor oncological prognosis, or poor performance status, placement of an external percutaneous biliary drainage catheter is most effective for palliation or to gain time for definitive treatment [15,82,83]. Possible complications of percutaneous biliary drainage are catheter dislodgement or obstruction, cholangitis, bile leak, extrahepatic hemorrhage, abscess formation, pneumothorax, and hemobilia [82,83.] Stent placement provides better quality of life for patients with incurable disease and relatively fair life expectancy, when compared to the presence of external drainage catheters [82]. Technical success is reported to be more than 90% and the clinical success 77-98% [85]. A frequently occurring complication of stent placement (5-25%) is stent occlusion [82]. This is treated by stent replacement or

placement of a percutaneous transhepatic internal-external drainage catheter. Galbladder outlet obstruction can be treated by cholecystectomy or percutaneous cholecystostomy, dependant on the ability of the patient to undergo surgery [15].

Urinary tract obstruction

Patients with retroperitoneal or pelvic malignant lesions can develop urinary tract obstruction [12,13,86]. Pelvic cancers such as prostate carcinoma, cervical cancer, and bladder carcinoma can cause bladder outlet obstruction [12,13]. Retroperitoneal malignancies, such as lymphoma, sarcoma, and metastatic lymphadenopathy from pelvic cancers, can cause ureteric obstruction. Large pelvic masses, such as ovarian carcinoma and pelvic sarcoma can result in bilateral ureteric obstruction. Obstruction is caused by either extramural compression or direct tumor invasion of the ureters, most frequently distal to the level of the common iliac vessels [12]. Benign causes for acute obstruction of the urinary tract in cancer patients can be fibrosis or pelvic inflammatory disease after surgery, catheter induced edema, or strictures after radiation therapy [86].

Patients with urinary tract obstruction present with flank pain and sudden anuria, sometimes alternating polyuria and progressive rise in serum creatinin [13]. Obstruction of the urinary tract can lead to hydronephrosis and subsequent infection and/or renal failure [13,86]. Patients with malignant obstruction are usually in poor condition with advanced metastatic disease, and palliative decompression can be performed [87].

Management

The aim of decompression is to secure renal function [88]. There is no indication for invasive laparotomy in cases of urinary tract obstruction. Decompression of the obstruction can be achieved by percutaneous nephrostomy catheters or an ureteric stent for obstructions of the upper urinary tract, and a suprapubic or transurethral bladder catheter in case of lower urinary tract obstruction [12,13,87,88]. When patients have a short life expectancy of only a few days or weeks and already significant renal failure, palliative pain control and refraining from any interventions may be the only suitable treatment [15].

Airway obstruction

Benign causes of the upper or lower airways in cancer patients include food or foreign body aspiration, airway edema or hemorrhage, angioedema, tracheal stenosis, and infections [13]. Malignant causes are intraluminal tumor growth or by extrinsic compression of the airway by tumors of the head, neck, and lung [13,21,23,89]. Dyspnea, cough, and wheezing are commonly the only early symptoms of airway obstruction [13,21,23]. If dyspnea occurs at exercise, the intraluminal diameter of the airway is usually decreased to about 8 mm [13]. However, if dyspnea occurs in rest, usually accompanied by stridor and/or retraction, and use of accessory muscles, immediate action is necessary since the airway diameter is expected to be critically narrow and less than 5 mm [13,21].

Management

A tracheotomy can be lifesaving in the acute setting for patients with an obstruction proximal to the larynx [13]. Semi-acute tracheostomy or intubation may be necessary [23,89]. Bronchoscopy with tumor debulking, ablation, or stenting are options for relief of more distal obstructions [13,89]. Steroids, chemotherapy or external beam radiation therapy may be helpful as well [13,21,23,89]. In case of extrinsic compression, stent placement is the preferred method of palliation [13,21,89]. Extensive surgical exploration of the obstruction is seldom performed because of the invasiveness of the procedure and the very poor prognosis in case of malignant airway obstruction [89]. For the same reasons, in cases of malignant obstruction, one should consider to refrain from any intervention or artificial ventilation, since many of them seem too invasive in cases of advances disease.

Malignant spinal cord compression

Malignant spinal cord compression (MSCC) is defined as compression, displacement, or encasement of the dural sac by spinal epidural metastases or locally advanced cancer and occurs in about 5-10% of all cancer patients [5,18,21]. MSCC is an oncologic emergency that becomes life threatening when it involves level C3 or higher, and requires immediate treatment to relieve pain and preserve neurological function [5,19,21].

Table 1. Possible locations, causes, and treatment options for symptoms of obstruction in cancer patients

Locations	Causes	Treatment options
Esophagus	• Intraluminal tumor presence or invasion • Extrinsic compression by tumor mass • Treatment-related edema • Initial worsening of obstructive symptoms due to chemo- or radiation therapy	• Conservative treatment (restoration of fluid and electrolyte balance, alternatives for feeding) • Endoscopic stent placement or ablation • No indication for surgery
Stomach	• Intraluminal tumor presence or invasion	• Conservative treatment (nasogastric decompression, restoration of fluid and electrolyte balance, alternatives for feeding) • Endoscopic stent placement • Surgical bypass or gastrectomy
Small intestine	• Postoperative adhesions • Postradiation strictures • Strangulation or hernia • Intraluminal tumor presence or invasion • Extrinsic compression by tumor mass • Peritoneal carcinomatosis	• Conservative treatment (nasogastric decompression, stimulation of stool passage, restoration of fluid and electrolyte balance, parenteral nutrition) • Laparotomy for adhesiolysis, bypass, bowel resection, or ileostomy
Colon/ rectum	• Intraluminal tumor presence or invasion • Extrinsic compression by tumor mass • Pseudo-obstruction (Ogilvie's syndrome) • Volvulus • Diverticulitis • Intussusception, • Anastomotic strictures after surgical resection	• Conservative treatment (nasogastric decompression, stimulation of stool passage, restoration of fluid and electrolyte balance, parenteral nutrition) • Endoscopic detorsion, stent placement, decompression, or ablation • Laparotomy for bowel resection, bypass, or ileo-/colostomy

Locations	Causes	Treatment options
Biliary tract	• Intraluminal tumor presence or invasion • Extrinsic compression by tumor mass • Postradiation strictures • Anastomotic strictures after surgical resection	• Percutaneous transhepatic or endoscopic (external or internal drainage) of biliary system • Endoscopic balloon dilatation or stent placement • Sphincterotomy • Surgical biliary-enteric bypass • Cholecystectomy or percuraneous cholecystostomy
Urinary tract	• Extrinsic compression by retroperitoneal or pelvic mass • Intraluminal tumor presence or invasion • Postsurgical fibrosis, structures, pelvic inflammatory disease • Catheter induced edema • Postradiation strictures	• Percutaneous nephrostomy catheter • Endoscopic ureteric stent placement • Suprapubic or transurethral bladder catheter • No indication for laparotomy
Airway	• Foreign body aspiration • Airway edema, hemorrhage, angioedema or infection • Tracheal stenosis • Intraluminal tumor presence or invasion • Extrinsic compression by tumor of head, neack, and lung	• Tracheotomy/-stomy, intubation • Bonchoscopy with tumor debulking, ablation, or stent placement • Steroids • Chemotherapy or external beam radiation therapy • No indication for extensive surgical exploration
Spinal cord	• Compression, displacement, or encasement of dural sac by epidural metastases or locally advanced cancer	• Glucocorticoids • External beam radiation therapy • Hormonal therapy, chemotherapy • Surgical decompression by laminectomy

Metastases from breast, renal, prostate and lung cancer are reported to account for the most common causes [5,18,19,21,23]. Symptoms of MSCC include local or radicular pain, worsening when lying down or during percussion of the vertebral bodies [5,18,19,23]. In a later stage, symptoms can be accompanied with neurological signs such as incontinence and loss of sensory function. Most patients will show abnormalities on plain radiographs of the spine, but the gold standard for assessing MSCC is magnetic resonance imaging (MRI).

Management

Management is effective in 90% of cases of early diagnosis and includes administration of high dose intravenous glucocorticoids with external beam radiation therapy, hormonal therapy, or chemotherapy [5,21,90]. The optimal dose and schedule of glucocorticoids and radiation therapy remain controversial in the literature [18,19]. Surgical decompression by laminectomy is indicated when pain and neurological symptoms are progressive despite initial treatment or spinal instability is present [5,18,19,21,23].

Infection

Patients with cancer frequently suffer from malnutrition and immune deficiency secondary to the disease or its treatment [82,91]. These factors can result in an increase in frequency, severity, and duration of infections, and also the development of infections caused by non-common pathogens [91].

Neutropenia is seen as a result of chemotherapy for leukemia, further, diminished function of T-lymphocyte and mononuclear phagocyte function is seen in patients with Hodgkin's and non-Hodgkin's lymphoma or in those receiving corticosteroids or chemotherapy. Alterations in B-lymphocyte function are seen in multiple myeloma, chronic lymphocytic leukemia, and secondary to chemotherapy. Typical manifestations of infections often change and may be masked due to immune deficiency [91,92]. In other cases, infections may manifest as severe life-threatening conditions, such as septic shock [91]. Immune deficient patients can develop infections of the gastrointestinal tract, such as perianal or perirectal abscesses, severe

mucositis, candidiasis, neutropenic enterocolitis and other intraabdominal infections [29,91,92].

Neutropenic enterocolitis is a life threatening condition and has been associated with acute lymphatic leukemia and chemotherapy [29,92,93]. It is a transmural inflammatory condition of the right colon and particularly the cecum, in the setting of myelosuppression and profound neutropenia [15,29,93]. However, it is also reported to affect the transverse and descending colon, and even the rectum [94]. It is thought to be caused by ischemia due to distention, leukemic infiltration of the bowel wall, direct toxic effects of chemotherapy, and bacterial invasion of the bowel wall after change in bowel flora [15,29]. The cecum is a poorly vascularised, often most dilated part of the bowel, and therefore at greatest risk to be affected in case of increased intraluminal pressure [15,93]. Symptoms include abdominal distention, diarrhea, fever and right lower quadrant tenderness and it may mimic acute appendicitis [15,29,95]. Characteristic findings on computed tomography are thickened bowel wall and also occasionally pneumatosis of the bowel wall [15,29,92]. Neutropenic enterocolitis can lead to bowel necrosis with perforation and sepsis [93,96].

Another cause of right lower quadrant pain can be appendicitis [29,92,97]. Typical symptoms and ultrasound findings of appendicitis can be masked in immune deficient patients, and thus, symptomatic patients may already have developed peritonitis [29]. A similar infection that can develop in cancer patients is acute cholecystitis, either resulting from immune deficiency, as complication of locoregional treatment of hepatic cancer, or cholelithiasis [82,92]. Due to masking of symptoms, acute cholecystitis may develop into gangrenous cholecystitis, emphysematous cholecystitis or even gallbladder perforation [82].

Management

Broad spectrum antimicrobial therapy is the initial management of choice for any infection in immune deficient patients and should be continued until neutropenia resolves or for a minimum of 10-14 days [91].

For neutropenic enterocolitis, initial therapy should be conservative with bowel rest, nasogastric suction, broad spectrum antibiotics, administration of fluid and electrolytes, and total parenteral nutrition [15,29,92]. Patients should improve as their white blood cell count returns to normal [29]. Many patients who are treated successfully with conservative treatment may develop a relapse of neutropenic enterocolitis during a next course of chemotherapy [15,29,93,95,98]. In the past some authors have recommended prophylactic bowel rest with total parenteral nutrition during consecutive chemotherapy and even elective right

hemicolectomy to prevent recurrence [95,98]. Prophylactic surgery is not common practice given the low incidence rates of fatal enterocolitis, the success rates of conservative treatment, the delay surgical interventions cause in chemotherapy cycles, and the invasiveness of the procedure [15]. If a patient doesn't improve after two to three days of conservative treatment, surgical resection of the right colon with primary or secondary anastomosis should be considered to prevent perforation [15,29,96]. Given the risks of surgery-related complications in patients with neutropenia, the consequences of a primary anastomosis after bowel resection and even the benefit of any surgical procedure must be questioned for patients who are septic and severely ill.

Uncomplicated acute appendicitis and cholecystitis treated by appendectomy and cholecystectomy have been reported to have unproblematic postoperative course [92,97]. However, for high-risk, immune deficient or severely ill patients, less invasive image guided percutaneous cholecystostomy must be considered as a bridge to surgery or as definitive treatment for cholecystitis [82]. In the presence of ascites, the transhepatic approach should be executed for percutaneous drainage, given the risk of leakage of bile and ascites with subsequent peritonitis for the transperitoneal approach. Indications for surgical drainage of perianal infections in patients with neutropenia is usually based on the white blood cell count and the development of an abscess, since this is dependent on the presence of leukocytes, and associated with better wound healing, fewer complications, and lower mortality [92].

Patients with an acute abdomen require immediate surgery for survival [29,96,97]. Even though mortality is high for immune deficient patients, mortality in immune deficient patients with peritonitis who are treated conservatively is reported to be 100%.

Perforation

When there is clinical evidence of pneumoperitoneum, perforation of a hollow organ must be suspected [12]. Regardless of treatment, perforation of the gastrointestinal tract with the concomitant infectious complications is a serious life-threatening emergency with mortality up to 100% in case of an oncontrolled perforation [15,99,100]. In addition, perforation of primary

tumor in the gastrointestinal tract is associated with a high risk on spread of tumor cells into the peritoneal cavity, worsening the patient's prognosis [15,99].

Perforation of the intestine can occur in cancer patients after prolonged obstruction [12,15,67,99]. Furthermore, it can result from localized intestinal wall replacement by tumor with subsequent tumor necrosis or from lack of normal mucosal integrity [15,99]. In tumors that are sensitive to chemotherapy, such as lymphoma, treatment responses in full-thickness intestinal wall tumor deposits with rapid necrosis of the malignant cells can lead to perforation [15]. Colorectal carcinoma and gastrointestinal lymphoma are malignancies that are associated with spontaneous perforation [12]. Perforation may result from complications of medicinal treatment such as steroids, NSAIDs, or from complications of chemotherapy, for example neutropenic enterocolitis and severe dehydration resulting in decreased bowel perfusion [15]. Last, some systemic agents, serving as anti-angiogenesic drugs such as bevacizumab for colorectal cancer, or sunitinib and imatinib for gastrointestinal stromal tumors (GIST), have been associated with intestinal perforation [12,15,101]. The evidence in the literature on the treatment of perforation induced by anti-angiogenic drugs is based on case series and there is no common approach for this emergency [102].

Perforation of other intraabdominal structures is also possible. Comparable to intestinal perforation, esophageal and gastric perforation can occur due to perforation of primary tumor, and due to secondary causes such as ischemia or treatment responses in gastrointestinal stromal tumors [15,38,103]. Malignant perforation of gastric cancer is often indicative of advanced disease [103].

Gallbladder perforation can be a complication of cholecystitis due to cholelithiasis, prolonged obstruction of the cystic duct, after biliary stent-placement, or locoregional ablation of hepatic cancer [82]. It is rarely associated with primary malignancy or metastases of the gallbladder. Symptoms can be similar to uncomplicated cholecystitis such as right upper quadrant pain or acute generalized peritonitis. Most gallbladder perforations are subacute with abscess formation or drainage into adjacent organs with fistula formation.

Management

Treatment of perforation of any organ depends on whether contents of the organ are spilled into the abdominal cavity, the patient's white blood cell count, and physical status [15,68,100]. It is based on drainage and control of the perforation with minimal stress for the patient, and following oncological principles.

Antimicrobial control is essential and broad spectrum antibiotics should be administered in any case. Urgent laparotomy is often necessary for the patient's survival in case of (suspection of) an uncontrolled perforation [15,46,99,103]. When there is a contained perforation with abscess formation and the absence of generalized peritonitis or sepsis, image-guided percutaneous drainage may be more suitable management [4,15]. In case of a primary non-metastasized tumor perforation of the intestine or stomach, surgery is justified and a formal resection with primary anastomosis or temporary ileo-/colostomy could remove both the primary tumor as well as the entire perforated segment [4,15,99]. Perforation of gallbladder is best treated by percutaneous drainage by cholecystostomy catheter or by directly draining the fluid collection as bridge to cholecystectomy [82].

For patients with poor performance who are septic and severely ill, and who are not expected to be fit for extensive surgical resections, a laparotomy with lavage of the peritoneum with or without proximal diversion by ileo-/colostomy, or an external drainage catheter is more appropriate [15,38]. This could allow resection at later stage. In case of perforation of intraabdominal structures during chemotherapy and subsequent neutropenia, mortality is very high due to infectious complications, even with aggressive broad spectrum antimicrobial therapy and surgical exploration [15]. Palliative care should be instituted for patients who are septic and have multi organ failure, who are not expected to benefit from surgery.

Bleeding

Hemorrhagic events in cancer patients may be caused by malignant disease or medical treatment [15,24,104]. Patients with visible bleeding can present with hematemesis, hemoptysis, hematochezia, melena, hematuria, vaginal bleeding, echymoses, petechiae, epistaxis, or ulcerated skin lesions [104]. Occult bleeding, i.e. intraperitoneal or retroperitoneal hemorrhage, can also develop [12]. Bleeding can occur in various stages of malignant disease and vary in severity [4,104]. It can originate from tumor invasion, local vessel damage, treatment response of tumor, or radiation injury. It can also result from coagulopathies or abnormalities in platelet function or number, induced by systemic therapy.

Severe intraabdominal bleeding can be caused by solid tumors, such as hepatocellular carcinoma, renal carcinoma, and melanoma [12]. Spontanous rupture of the spleen caused by lymphoma or leukemia can also result in severe intraabdominal bleeding [12]. Bleeding can occur from solid malignancies of the gastrointestinal tract and other hollow organs such as the bladder, as a result of tumor invasion into the organ or mucosa [24]. Risk factors for bleeding from solid tumors include large tumor size, peripheral or subcapsular location, and increased vascularity [12]. Direct vascular invasion, increased intratumoral pressure, increased venous pressure or portal hypertension, and decreased autoregulatory mechanisms within the tumor vessels, can cause spontaneous bleeding [12].

Some chemotherapeutic agents and anti-angiogenic targeted therapies, are associated with increased bleeding tendency, decreased wound healing, and gastric perforation [13,24]. Patients receiving radiation therapy for pelvic malignancies can develop lower gastrointestinal bleeding, and this may occur months to years after treatment [24]. NSAIDs, which are taken by many cancer patients as pain medication, are associated with an increased risk of gastrointestinal bleeding [24,104]. Coagulopathies, such as hyperviscosity syndrome or disseminated intravascular coagulation are possible causes of spontaneous bleeding in cancer patients [5,15,20,21,24]. Last, quantitative or qualitative platelet defects induced by liver failure, chemotherapy, hematological malignancies, or anticoagulants can be the underlying cause.

Management

In the acute setting, initial management of hemorrhage is based on hemodynamic monitoring, establishment of intravenous access, and fluid resuscitation or even transfusion of blood products if necessary [4,24,104]. Agents that advance bleeding or inhibit coagulation should be eliminated, and definite treatment of solid bleeding tumors should be initiated [24]. Prior to any intervention, if possible, identification of systemic abnormalities and localization of the bleeding source by (interventional) angiography or endoscopy is preferable [4,104].

Systemic interventions for bleeding include correction of underlying coagulopathies and platelet defects by administration of clotting factor, vitamin K, vasopressin, somatostatin analogues, antifibrinolytic agents or blood products [82,104]. Applying local pressure, hemostatic or vasoconstricting agents and dressings may provide in temporary measures for local bleeding from skin lesions, nose, vagina or rectum [104].

Endoscopy is an effective minimally invasive method for bleeding in the gastrointestinal tract, lungs, and bladder [4,24,104]. It can be used for localization, but also for hemostasis using injection of sclerosing agents, heater probe, electro- or photocoagulation. Nevertheless, sometimes it can be difficult to identify the location of the bleeding, and bleeding often recurs when it originates from the tumor site. Angiography and interventional radiologic embolization of blood vessels is minimal invasive, can be very effective, also for localization, and limits the need for laparotomy [4,104]. However, it is limited by multiple factors [104]; presence of a bleeding disorder, accessibility of the target blood vessels, subsequent ischemia of important non-target organs, and the availability of appropriate expertise. Radiation therapy can be considered for hemoptysis, bleeding from skin lesions, vagina, rectum and bladder and may be effective in 60-85% of cases [90,104].

Emergency surgery may be required to control severe bleeding with persistent hemodynamic instability despite attempts of resuscitation, failure of other therapy, and recurrent bleeding [4,24,103,104]. However, surgery is often difficult after a long trial of conservative treatment due to clinical deterioration after great blood loss or coagulopathies.

Pathological fractures

Bone injury can result from primary bone tumors or metastases from lung, prostate, breast, kidney, thyroid cancer and all kinds of other malignancies [15,105-107]. After radiation therapy, bone tissue can become hypovascular, hypocellular and hypoxic, and the bone has a decreased ability to replace the normal collagen and cellular losses [106]. Furthermore, androgen deprivation therapy, for example in the treatment of prostate cancer, is associated with development of osteoporosis [108]. Bone injury in cancer patients becomes emergent in case of pathological fractures, spinal cord compression, hypercalciemia, bone marrow infiltration and severe bone pain [105,107].

Management

Studies on the use of bisphosphonates have shown to have a positive effect on prevention of skeletal-related events in patients with bone metastases originating from breast or prostate

cancer, and multiple myeloma (up to 10% absolute risk reduction) [108-110]. Acute cancer related fractures are an indication for surgery and are treated with internal fixation or joint prostheses dependent on the fracture type and underlying malignant cause (i.e. primary tumor or metastatic) [15,107]. However, healing rates of pathological fractures are dependent on the type of malignancy and have been reported to be between 0% and 67% [107]. Whatever fixation device is used, it is recommended to use a device that will last as long as the life expectancy of the patient, and stabilizes the entire diseased bone at once. Additional radiation therapy is often indicated for local control and quality of life. Opinions differ on the best radiation scheme for bone metastases. Single dose regimens have been compared to multifraction regimens and no differences were noted for symptomatic improvement. Different regimens may be indicated for patients with short or longer life expectancy. For palliation of severe bone pain, radiation therapy and bisphosphonates may be effective [15,107,109]. The exact mechanism of action of radiation therapy on bone pain is unknown [107].

Patient selection, palliative care, and quality of life

No cancer patient is equal in potential to recover from extensive procedures in the acute setting. There are many factors which can't be measured or compared in randomized studies that play a role in the process of decision making concerning treatment for surgical emergencies. The patient's performance status, cancer stage and life expectancy, type and severity of the emergency, and - most importantly - the patient's and families wishes regarding invasiveness of treatment, are major determinants for the choice of therapy and clinical outcome [15,104]. These determinants are individually diverse and it is difficult to define prognostic factors and the right treatment for cancer patients in an emergency setting [111]. When possible, in any emergency situation it is important to create the opportunity for diagnostic methods in order to identify the cause of the emergency, and for multidisciplinary evaluation.

In the absence of curative treatment options, the aim of palliative therapy should be to reduce symptoms without reducing the quality of life [83]. The risk of intervention related complications may be greater than a beneficial outcome and may even reduce survival.

When interventions are insufficient in patients with poor condition, refraining from invasive therapy with palliation of discomfort will be the only appropriate option left [15]. Therapy for any emergency depends on the individual case and ethical considerations regarding extensive procedures, quality of life, and continuation of treatment [112]. It is essential to inform the patient and family about the prognosis of the condition, treatment options, and the expected impact and benefit of treatment. Personalized policies and a multidisciplinary approach are necessary for optimal treatment and/or palliation, to suffice the patient's and families wishes, and to prevent unnecessary invasive procedures at the end of life.

Summary

To our knowledge, this is the first review on surgical emergencies in oncology. There are various surgical emergencies that can occur in cancer patients and these can have either benign or malignant origin. The most frequent surgical emergency experienced by cancer patients is obstruction of the gastrointestinal tract. Obstruction can also develop in other structures, such as the urinary tract, airway, or spinal cord. Other surgical emergencies include perforation of the gastrointestinal tract, bleeding events, infections due to immune deficiency, and pathological fractures.

The patient's performance status, cancer stage and prognosis, type and severity of the emergency, and - most importantly - the patient's wishes regarding invasiveness of treatment are essential during the decision making for optimal management. The complications of the oncologic emergency can be more life threatening than the risks of an intervention, whereas for others, the intervention itself can cause worse outcome and shorten survival. The institution of palliative (terminal) care may be more appropriate for some patients. Personalized policies and a multidisciplinary approach are necessary for optimal treatment and/or palliation, to suffice the patient's and families wishes, and to prevent unnecessary invasive procedures at the end of life.

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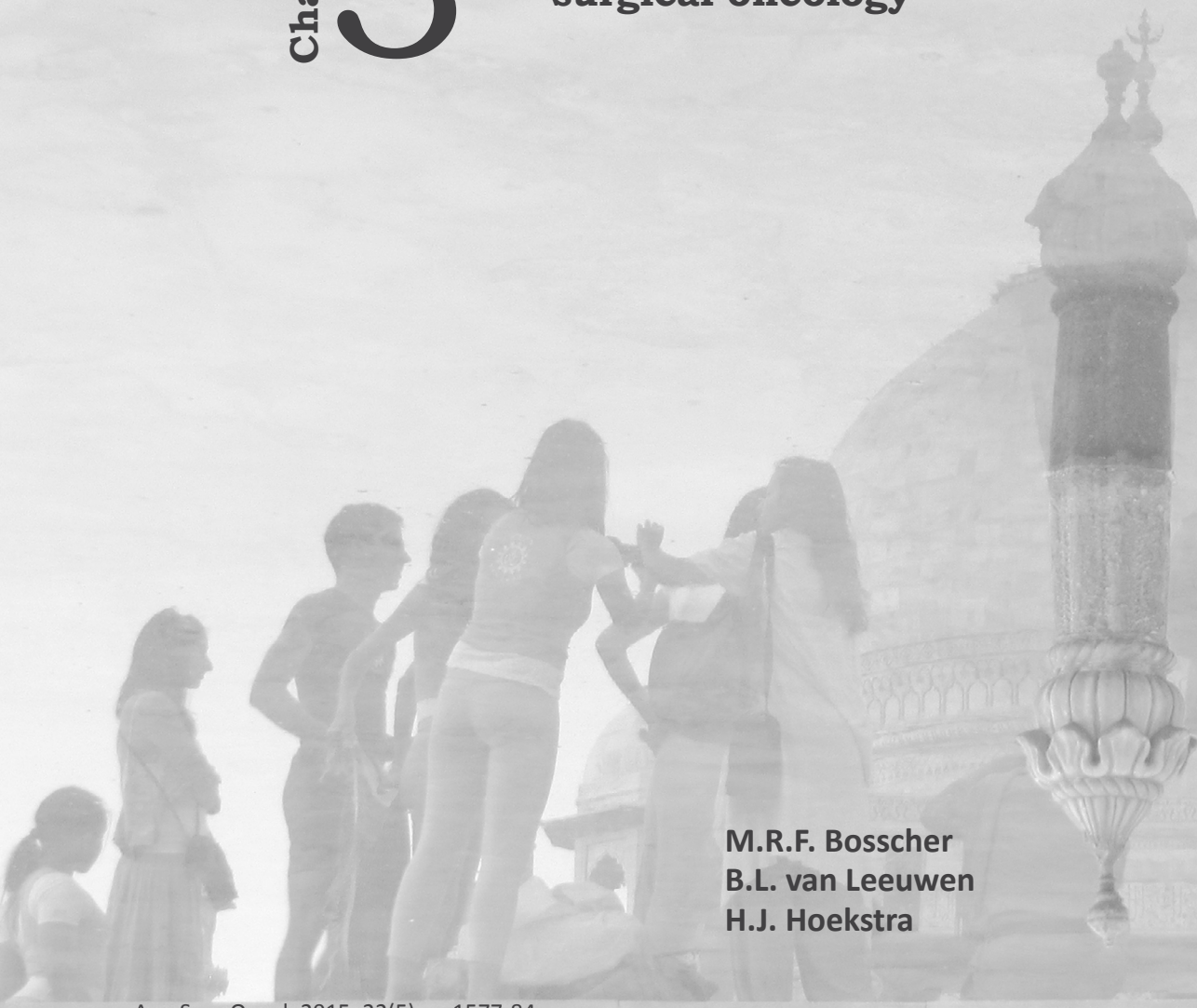
Chapter 3

Mortality in emergency surgical oncology



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Abstract

Purpose

Cancer patients can experience problems related to their disease or treatment. This study evaluated reasons for presentation at the emergency room (ER) and outcome of surgical oncology patients.

Methods

A retrospective chart review for all surgical oncology patients who presented at the ER of the University Medical Center Groningen for surgical consultation between October 1, 2012, and March 31, 2013.

Results

A total of 200 cancer patients visited the ER for surgical consultation, 53.5% with complications of (previous) cancer treatment, 25.5% with symptoms caused by malignant disease, and 21.0% with symptoms not related to cancer or cancer treatment. The 30-day mortality rate for patients with progressive disease was 25.5%, and overall mortality rate was 62.8%. The most frequent reason for ER presentation was intestinal obstruction (26.5%), of which 41.5% was malignant. Most cancer patients (59.5%) did not undergo surgery during follow-up. The 30-day mortality for these patients was 14.3%, and overall mortality was 37.8%. Most patients that died within the first 30 days after ER presentation had not undergone any surgery after presentation (89.5%).

Conclusions

There is great variation in mortality rates for cancer patients presenting at the ER for surgical consultation. The mortality in this study was greatest for patients with progressive disease (30-day mortality 25.5% and overall mortality 62.8%), and the majority of patients who died within 30 days (89.5%) had not undergone surgery after ER presentation. Surgery should only be performed in the acute setting when essential and when the expected outcome is favorable for the patient.

Introduction

Cancer patients can experience problems related to their disease or cancer treatment at all stages of the disease, leading to presentation at the emergency room (ER) [1, 2]. An oncologic emergency is defined as an acute, potentially life threatening condition in a cancer patient that has developed directly or indirectly as a result of cancer or cancer treatment [2, 3]. Patients can present with symptoms caused by primary malignancy, disease progression, recurrence, or complications of surgery, radiation therapy, chemotherapy, and immune deficiency [1, 4-9]. Cancer patients admitted through the ER generally have advanced disease and higher mortality compared with patients admitted or evaluated electively [1, 6, 10-14]. The number of visits to the ER increases near the end of life [11]. In a systematic review, Vandyk et al. explored range, prevalence, and outcome of treatment-related or disease-related symptoms for cancer patients presenting to the emergency department [8]; they found variation and inconsistency in the reporting of symptoms and mortality, with the latter varying between 1% and 67%.

A certain proportion of oncologic emergencies may require surgical expertise and treatment. A few studies have evaluated surgical emergencies in oncology [9, 15-17]. Surgical emergencies include bleeding, obstruction, gastrointestinal perforation, infectious complications due to immune deficiency, and postoperative complications, such as infection, anastomotic leak, wound healing disturbances or intestinal obstruction [1, 3, 9, 17, 18]. Cancer patients requiring emergency surgery have a longer hospital stay and worse survival rates compared with those undergoing elective surgery [1, 15, 19]. Emergency surgery should be used to control emergency situations; however, for cancer patients, other non-operative forms of treatment should also be considered [15, 16, 18]. These can be used as palliative treatment or bridge to surgery at a later stage if the patients' physical status does not allow surgical intervention.

The outcome of care in cancer patients with emergency presentation is worth exploring in order to provide evidence for (multidisciplinary) decision-making and improved quality of care in the acute setting [8, 10, 20]. In this study, we evaluated the reasons for presentation at the ER for surgical consultation of cancer patients, surgical interventions after presentation, and the mortality rate.

Methods

In accordance with institutional guidelines, a retrospective chart review was performed for patients who presented at the ER of the University Medical Center Groningen (UMCG), between October 1, 2012, and March 31, 2013.

Initial triage at the ER of the UMCG is performed by a nurse, who triages the patients to be consultated by the different medical or surgical specialties. After triage, physicians can request consultation of other specialties. The charts of patients who were triaged for general surgery and surgical oncology were reviewed. When available, all patients with a history of cancer, as well as patients with a primary presentation of malignant disease at the ER were included.

Patients were divided into three different categories according to their final diagnosis, (1) complication of (previous) cancer treatment, (2) caused by malignant disease, and (3) visit not related to cancer or cancer treatment. The patients' symptoms were documented, whether the patient was admitted, duration of emergency admission, and if the patient underwent any surgical intervention during follow-up.

Symptoms of intestinal obstruction with clinical evidence of tumor presence were regarded as malignant intestinal obstruction. All other cases of (transient) intestinal obstruction in the absence of signs of disease activity were regarded as benign. Adhesive bowel obstruction or strictures after previous abdominal surgery was regarded as related to cancer treatment. Symptoms interpreted as constipation in the absence of previous abdominal surgery were considered as intestinal obstruction neither related to cancer or cancer treatment. Other symptoms, that could not be related to (surgery performed as) cancer treatment, immune deficiency, or cancer, were classified as not related to cancer or cancer treatment. Emergency surgery was defined as a surgical intervention which was performed non-electively.

Follow-up ended September 30, 2013. At final follow-up, charts of all patients were reviewed for correspondence regarding activity of malignant disease, mortality, and surgical procedures performed during the follow-up period after presentation at the ER. Data analysis was performed using IBM SPSS statistics 22.

Results

Between October 1, 2012, and March 31, 2013, 200 cancer patients, median age 64 (range 18 – 89) years, 109 males (54.5%) and 91 females (45.5%), visited the ER for surgical consultation. In total, 114 patients (57.0%) were admitted through the ER, median duration of emergency admission was 7 (range 1-71) days. Median follow-up was 408 (range 0 - 547) days.

There were 107 patients (53.5%) who presented with complications of cancer treatment. In this group 97 patients (90.7%) presented with complications after surgery and/or abdominal radiation therapy, and 10 patients (9.4%) with complications related to chemotherapy. Furthermore, 51 patients (25.5%) presented with symptoms caused by malignant disease, of whom 6 patients (11.8%) presented with symptoms leading to diagnosis of cancer. The remaining 45 patients were previously diagnosed with cancer. Finally, the visit of 42 patients (21.0%) with a medical history of malignant disease was not related to their cancer or previous cancer treatment. Table 1 provides an overview of patient characteristics within the different categories.

The 30-day mortality rate for all patients was 9.5%, and overall mortality at final follow-up was 32.5%. The median survival was 128 (range 0 – 489) days. At final follow-up, 17.5% of all patients were Alive With Disease (AWD) and 31.5% died of progressive malignant disease (Death Of Disease – DOD). Further, 45.0% were alive and had No Evidence of Disease (NED), and 1 patient (0.5%) died without signs of disease activity (Death Other Causes - DOC). For 5.5% of all patients there was no recent oncologic correspondence. Figure 1 visualizes the rates of disease activity at final follow-up within the different categories.

The 30-day mortality rate for the patients who presented with symptoms caused by malignant disease was 25.5%, and the overall mortality rate at final follow-up was 62.8%. Median survival was 69 (range 0-436) days. The most prominent types of cancer were small or large bowel adenocarcinoma (28.5%), genitourinary tract (12.0%), and gastric, esophageal, or laryngeal cancer (10.0%).

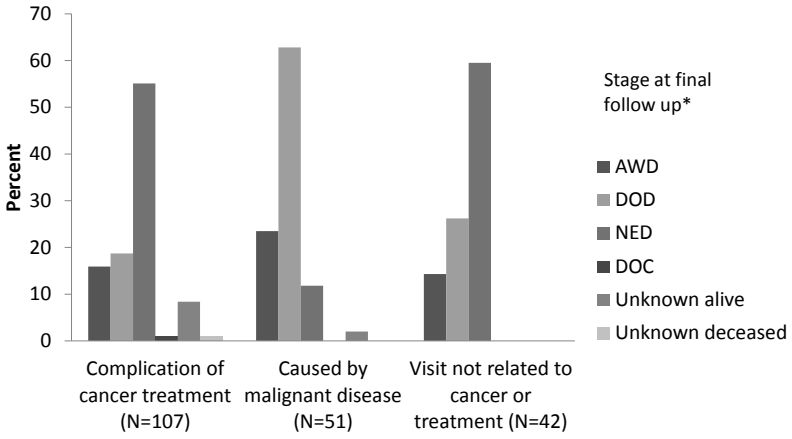
Table 1. Characteristics of cancer patients presenting at the ER for surgical consultation

	Total	Complication of cancer treatment	Caused by malignant disease	Visit not related to cancer or treatment
Total (%)	200 (100)	107 (53.5)	51 (25.5)	42 (21.0)
Median age (years)	64 (18-89)	63 (18-89)	65 (26-84)	64 (19-88)
Gender				
Male (%)	109 (54.5)	58 (54.2)	27 (52.9)	24 (57.1)
Female (%)	91 (45.5)	49 (45.8)	24 (47.1)	18 (42.9)
Type of malignancy				
Small bowel, colorectal (%)	57 (28.5)	36 (33.6)	15 (29.4)	6 (14.3)
Genitourinary (%)	24 (12.0)	11 (10.3)	6 (11.8)	7 (16.7)
Esophageal, gastric, laryngeal (%)	20 (10.0)	13 (12.1)	4 (7.8)	3 (7.1)
Melanoma (%)	18 (9.0)	11 (10.3)	7 (13.7)	-
Breast (%)	17 (8.5)	12 (11.2)	1 (2.0)	4 (9.5)
Hematologic (%)	15 (7.5)	7 (6.5)	2 (3.9)	6 (14.3)
Liver, pancreatic, cholangio (%)	8 (4.0)	2 (1.9)	6 (11.8)	-
Non melanoma skin cancer (%)	9 (4.5)	4 (3.7)	1 (2.0)	4 (9.5)
Soft tissue sarcoma (%)	8 (4.0)	3 (2.8)	3 (5.9)	2 (4.8)
Other (%)	24 (12.0)	8 (7.5)	6 (11.8)	10 (23.8)
Stage of treatment before presentation				
No cancer (%)	6 (3.0)	-	6 (11.8)	-
Active disease				
• Diagnostic/staging phase (%)	8 (4.0)	2 (1.9)	4 (7.8)	2 (4.8)
• Receiving treatment with curative intent (%)	60 (30.0)	43 (40.2)	10 (19.6)	7 (16.7)
• Palliative stage (%)	37 (18.5)	10 (9.4)	20 (39.2)	7 (16.7)
NED after being treated for cancer in the past (%)	89 (44.5)	52 (48.6)	11 (21.6)	26 (61.9)
Previous cancer treatment				
Yes (%)	183 (91.5)	107 (100)	39 (76.5)	37 (88.1)
No (%)	17 (8.5)	-	12 (23.5)	5 (11.9)
Emergency admission (%)	114 (57.0)	51 (47.7)	38 (74.5)	25 (59.5)
Median duration of emergency admission (days)	7 (1-71)	8 (1-51)	10 (1-71)	4 (1-26)

	Total	Complication of cancer treatment	Caused by malignant disease	Visit not related to cancer or treatment
Surgery (%)	81 (40.5)	44 (41.1)	22 (43.1)	15 (35.7)
• Emergency surgery same admission (%)	46 (23.0)	24 (22.4)	10 (19.6)	12 (28.6)
• Elective surgery related to presentation (%)	17 (8.5)	5 (4.7)	10 (19.6)	2 (4.8)
• Emergency surgery other reason (%)	6 (3.0)	4 (3.7)	2 (3.9)	-
• Elective surgery other reason (%)	12 (6.0)	11 (10.3)	-	1 (2.4)
No surgery during follow up (%)	119 (59.5)	63 (58.9)	29 (56.9)	27 (64.3)
Deceased during follow up (%)	65 (32.5)	22 (20.6)	32 (62.8)	11 (26.2)
• Within 30 days (%)	19 (9.5)	3 (2.8)	13 (25.5)	3 (7.1)
• 30 days - 6 months (%)	21 (10.5)	6 (5.6)	12 (23.5)	3 (7.1)
• 6 months – 1 year (%)	15 (7.5)	7 (6.5)	4 (7.8)	4 (9.5)
• 1 year – 1.5 years (%)	10 (5.0)	6 (5.6)	3 (5.9)	1 (2.4)
Median survival of deceased (days)	128 (0-489)	246 (2-474)	69 (0-436)	159 (1-489)
Median follow up (days)	408 (0-547)	417 (2-547)	196 (0-546)	428 (1-541)
Disease activity at follow up *				
Yes (%)	98 (49.0)	37 (34.6)	44 (86.3)	17 (40.5)
• AWD (%)	35 (17.5)	17 (15.9)	12 (23.5)	6 (14.3)
• DOD (%)	63 (31.5)	20 (18.7)	32 (62.8)	11 (26.2)
No (%)	91 (45.5)	60 (56.1)	6 (11.8)	25 (59.5)
• NED (%)	90 (45.0)	59 (55.1)	6 (11.8)	25 (59.5)
• DOC (%)	1 (0.5)	1 (0.9)	-	-
Unknown (%)	11 (5.5)	10 (9.3)	1 (2.0)	-
• Alive (%)	10 (5.0)	9 (8.4)	1 (2.0)	-
• Deceased (%)	1 (0.5)	1 (0.9)	-	-

* AWD: Alive With Disease, DOD: Death Of Disease, NED: No Evidence of Disease, DOC: Death Other Causes

Figure 1. Disease activity at final follow up within subgroups of cancer patients presenting at the ER for surgical consultation. **AWD* alive with disease*, DOD death of disease, NED no evidence of disease, DOC* death other causes



Classification of reason for presentation at the Emergency Room

The most frequent reason for presentation of cancer patients at the ER of the UMCG was intestinal obstruction (26.5%); the majority was regarded as benign (58.5%), and 41.5 % due to a malignant cause. Table 2 provides an overview of the symptoms of cancer patients presenting at the ER. For patients presenting with malignant intestinal obstruction, 30-day mortality was 9.1%, and the overall mortality at final follow-up was 54.5%. For patients presenting with benign intestinal obstruction, 30-day mortality was 3.2%, and overall mortality at final follow-up was 12.9%.

After emergency presentation, 81 patients (40.5%) underwent surgery during follow-up; 46 patients (23.0%) underwent emergency surgery during the same emergency admission, and 17 (8.5%) underwent elective surgery related to the reason for presentation at the ER. Further, 18 (9.0%) patients underwent surgery during follow-up, not related to the initial

presentation at the ER. Table 3 gives an overview of surgical procedures for the most frequent reasons for presentation. Most patients did not undergo surgery during follow-up (59.9%). When patients underwent surgery, the procedures that were most frequently performed were drainage of abscesses, excision of fistula or wound debridement (10.5%). Of the patients presenting with benign intestinal obstruction, 29.0% underwent a laparotomy for benign resection, adhesiolysis or anastomotic leak. Of the patients with malignant intestinal obstruction, 31.8% underwent a palliative bypass of ileo-/colostomy with of without tumor or bowel resection.

Table 2. Symptoms of cancer patients presenting at the ER for surgical consultation

	Total N (%)	Complication of cancer treatment N (%)	Caused by malignant disease N (%)	Visit not related to cancer or treatment N (%)
Total	200 (100)	107 (100)	51 (100)	42 (100)
Intestinal obstruction	53 (26.5)	21 (19.6)	22 (43.1)	10 (23.8)
• Benign	31 (58.5)	21 (100)	-	10 (100)
• Malignant	22 (41.5)	-	22 (100)	-
Wound infection, abcess, fistula	52 (26.0)	45 (42.1)	-	7 (16.7)
Other infections, thrombosis	17 (8.5)	10 (9.4)	-	7 (16.7)
Clinical deterioration, pain, renal failure, neurological symptoms	17 (8.5)	-	17 (33.3)	-
Gastrointestinal infection, pancreatitis	15 (7.5)	1 (0.9)	2 (3.9)	12 (28.6)
Problems with feeding tube, drain, indwelling catheter	14 (7.0)	13 (12.4)	-	1 (2.4)
Abdominal sepsis, intestinal perforation, neutropenic enterocolitis	11 (5.5)	6 (5.6)	1 (2.0)	4 (9.5)
Pain from wound, scar, ileo-/colostoma without infection	8 (4.0)	7 (6.5)	-	1 (2.4)
Biliary obstruction	8 (4.0)	1 (0.9	7 (13.7	-
Bleeding	5 (5.2)	3 (2.8)	2 (3.9)	-

Table 3. Surgical procedures following emergency presentation of cancer patients at the ER for the most frequent symptoms of presentation

	Total N (%)	Intestinal obstruction, benign N (%)	Intestinal obstruction, malignant N (%)	Wound infection, abscess, fistula N (%)	Other symptoms N (%)
Total	200 (100)	31 (100)	22 (100)	52 (100)	95 (100)
No surgery during follow up	119 (59.9)	19 (61.3)	9 (40.9)	26 (50.0)	65 (68.4)
Drainage of abscess, excision of fistula, wound debridement	21 (10.5)	-	-	13 (25.0)	8 (8.4)
Laparotomy for benign resection, adhesiolysis or anastomotic leak	19 (9.5)	9 (29.0)	1 (4.6)	2 (3.9)	7 (7.4)
Tumor resection or excision	14 (7.0)	1 (3.2)	2 (9.1)	6 (11.5)	5 (5.3)
Laparotomy for palliative bypass, ileo-/colostomy with/without resection	12 (6.0)	2 (6.5)	7 (31.8)	1 (1.9)	2 (2.1)
Cholecystectomy, appendectomy	7 (3.5)	-	-	2 (3.9)	5 (5.3)
HIPEC	4 (2.0)	-	3 (13.6)	-	1 (1.1)
Lymph node dissection	2 (1.0)	-	-	2 (3.9)	-
Splenectomy	1 (0.5)	-	-	-	1 (1.1)
Vascular surgery	1 (0.5)	-	-	-	1 (1.1)

Figure 2. Surgery during follow up and mortality of cancer patients following presentation at the ER for surgical evaluation

Table 4. Outcome of surgical procedures performed during follow up after presentation at the ER for surgical evaluation

	Total	Palliative stage before inclusion	Emergency surgery	30-day mortality	Deceased during FU	NED at final FU
Total (%)	200 (100)	34 (17.0)	46 (23.0)	19 (9.5)	64 (32.0)	91 (45.5)
No surgery during follow up (%)	119 (100)	18 (15.1)	-	17 (14.3)	45 (37.8)	57 (47.9)
Drainage of abscess, excision of fistula, wound debridement (%)	21 (100)	4 (19.0)	14 (66.7)	-	6 (28.6)	10 (47.6)
Laparotomy for benign resection, adhesiolysis or anastomotic leak (%)	19 (100)	3 (15.8)	18 (94.7)	1 (5.3)	4 (21.1)	10 (52.6)
Tumor resection or excision (%)	14 (100)	1 (7.1)	1 (7.1)	-	1 (7.1)	5 (35.7)
Laparotomy for palliative bypass, ileo-/colostomy with or without resection (%)	12 (100)	5 (41.7)	8 (66.7)	1 (8.3)	6 (50.0)	3 (25.0)
Cholecystectomy, appendectomy (%)	7 (100)	2 (28.6)	5 (71.4)	-	-	4 (57.1)
HIPEC (%)	4 (100)	-	-	-	2 (50.0)	-
Lymph node dissection (%)	2 (100)	1 (50.0)	-	-	-	-
Splenectomy (%)	1 (100)	-	-	-	-	1 (100)
Vascular surgery (%)	1 (100)	-	-	-	-	1 (100)

For the patients who did not undergo surgery during follow-up after presentation, 15.1% was already in a palliative phase before presentation at the ER, the 30-day mortality was 14.3% and overall mortality at final follow-up was 37.8% (Table 4. and Figure 2). Of the patients who underwent emergency surgery, 26.1% was in a palliative phase before inclusion, 30-day mortality was 2.2% and overall mortality at final follow-up was 26.1%. Of the patients undergoing elective surgery, 5.9% was in a palliative phase before inclusion, 30-day mortality was 5.9%, and overall mortality was 35.3%. Most patients who died within the first 30 days after presentation (89.5%) had not undergone any surgical procedure after presentation at the ER. One patient underwent a laparotomy for intestinal perforation and died of sepsis postoperatively. The other patient died due to cardiac arrest during elective surgery.

Discussion

Cancer patients can experience problems requiring emergency evaluation, and some of these problems may require surgical treatment [1, 18, 21]. In this study, of all cancer patients who presented at the ER for surgical consultation, 53.5% presented with complications of (previous) cancer treatment, and 25.5% presented with symptoms caused by malignant disease. This means that the majority of cancer patients at the ER presents with oncologic emergencies, since only 21.0% of all cancer patients presented with symptoms that could not be related to malignant disease or cancer treatment.

The overall mortality rate after presentation at the ER for surgical consultation was 32.5% after a median follow-up of 408 days. The varying mortality rates between the different subgroups is in accordance with the literature [8]. Nevertheless, in this study, the overall mortality of 62.8% for patients presenting with symptoms caused by malignant disease, is in the upper range of reported mortality for cancer patients after emergency presentation in the literature (1%-67%), even after a relatively short follow-up. The 30-day mortality for the category of cancer patients who presented with symptoms caused by malignant disease was 25.5%. Considering the overall mortality of 62.8% within this category, this means that more than one-third of all patients who were deceased during the follow-up period (i.e. 40.6%) died within the first 30 days. These results underscore the importance of awareness regarding the occurrence of oncologic emergencies. The mortality rates found in this study confirm the fact that all cancer patients require special attention at the ER, regardless of the reason for presentation.

At final follow-up, 45.5% of all patients were NED. Nevertheless, this was only for 11.8% of patients who presented with symptoms caused by malignant disease. The remaining 86.3% were AWD, or had died of progressive disease (DOD). Patients who presented with symptoms caused by malignant disease, clearly had a worse outcome than patients presenting for complications of cancer treatment or other reasons. Regarding the rate of disease activity within this group when the study ended, the overall mortality is expected to increase when the follow-up period will be extended.

In some emergency oncology situations, determining whether symptoms are caused by disease progression, the effects of cancer treatment, or non-oncologic causes is difficult [16]. Time for diagnostic methods for definite diagnosis is not always available [3, 16]. However, medical decisions have to be made within a certain time frame to guarantee optimal patient care. It is important to have the right knowledge and judgment for institution of proper treatment. The main reasons for emergency surgery in oncology are bowel obstruction, gastrointestinal perforation, and hemorrhage [3, 17, 18, 22, 23]. Furthermore, patients with acute or chronic leukemia, and patients who receive chemotherapy, can suffer from complications due to cytopenia or immunosuppression, requiring emergency surgical treatment [9, 18, 24, 25].

In this study, intestinal obstruction was the most frequent symptom for surgical consultation at the ER. More than one-third of cases of intestinal obstruction were proven to have a malignant cause (41.5%). In 40.9% of cases with malignant causes, patients were treated conservatively, and 59.1% underwent surgery in either an emergent or elective setting. For benign causes, 61.3% of patients were treated conservatively and 38.7% underwent surgery during the follow-up period. In the literature, benign causes have been reported to account for 18% up to 55% of cases of small bowel obstruction, in contrast to colorectal obstruction, with a reported 80% for malignant origin [23, 26-29]. For both conditions, the combination of malignant origin and emergency presentation is associated with advanced disease and worse outcome [3, 30-33]. Mortality in this study was high for patients with malignant intestinal obstruction (30-day mortality 9.1%, and overall mortality at final follow-up 54.5%), compared with patients with benign origin (3.2% and 12.9% respectively).

For patients who did not undergo surgery after presentation, 30-day mortality was 14.3% and the overall mortality at final follow-up was 37.8%. The 30-day mortality rates for patients undergoing elective surgery or emergency surgery related to the presentation at the ER were 5.9% and 2.2% respectively, and overall mortality rates at final follow -up were 35.3% and 26.1%. Surprisingly, the 30-day mortality and overall mortality rates were less after emergency surgery compared with elective surgery related to the reason for presentation at the ER, despite the fact that about five times as many patients who underwent emergency surgery (26.1%) were in a palliative phase compared with the patients who underwent elective surgery (5.9%).

In the literature, mortality and survival have been reported to be worse after emergency surgery compared with elective surgery because of the more advanced disease in the former group [1, 15, 19, 34]. Barnett et al. described a 30-day mortality of 11% after emergency surgery compared with 5% after elective surgery for colorectal cancer, and a 2-year survival of 42% and 65% respectively [1]. These studies mainly highlight the difference in mortality between emergency and elective procedures. More importantly, mortality in this study was greatest for patients who did not undergo any surgical intervention after presentation. The majority (89.5%) of all patients who died within 30 days had not undergone surgery after emergency presentation.

The difference in mortality rates in this study between patients who did not undergo any surgery after emergency presentation, and patients undergoing emergency or elective surgery, is possibly due to a proper assessment of the patients' physical status in an emergency setting; i.e. performing emergency surgery on the patients who benefit from this procedure, even if they are already in a palliative stage, bridging patients to elective surgery when possible, and refraining patients with more advanced disease and worse condition from any surgery [18, 35-37]. On the other hand, it could be possible that the difference in mortality rates is due to a withholding policy in regards to performing surgery, although it could have been favorable for survival of the patient.

In many situations multiple medical disciplines are involved during emergency admission, due to concurrent issues of attention. Multidisciplinary evaluation of the cancer patient, and defining the patient's performance score on admission would be beneficial for better risk assessment and determination of further treatment to prevent unnecessary invasive procedures at the end of life [18].

Limitations of this retrospective study were that it is impossible to detect all cancer patients that experienced surgical emergency symptoms and presented at the ER, especially those with a primary presentation. We did not include patients admitted through the outpatient clinic or patients with neurological symptoms and/or (pathological) fractures requiring admission for neurosurgery or orthopedic surgery. Last, categorizing a very heterogeneous group of patients with different types of malignancies and different types of symptoms into only a few categories was difficult. However, it will provide more overview of the reasons for presentation in surgical oncology and predictors of final surgical oncology outcome [38-40].

Even with the ample selection of possible treatment, the patients' prognosis, performance and quality of life should be taken into account when determining policy and treatment [15, 18, 39, 40]. Surgery should only be performed when essential and when the expected outcome is favorable for the patient [1, 15, 16, 35, 39]. A multidisciplinary approach is required, and other forms of treatment should be considered for cancer patients with poor prognosis [1, 15, 16, 41]. Patients' preferences should be taken into account when determining the intensity of care at the end of life [42]. When no intervention will be meaningful, palliative care should be provided in hospital or home situations. General practitioners can provide many elements of care [43-46]. Further prospective research is needed to gain a more detailed insight in prognostic factors and optimal treatment for cancer patients in emergency situations.

Conclusions

Of all cancer patients who presented at the ER for surgical consultation, 53.5% presented with complications of cancer treatment, 25.5% with symptoms caused by malignant disease, and only 21.0% with symptoms that could not be related to malignant disease or cancer treatment. Mortality was highest for patients who presented with symptoms caused by malignant disease, and more than one-third of the deceased patients died within the first 30 days after emergency presentation. Intestinal obstruction was the most frequent symptom, and more than one-third were proven to be malignant. The mortality in this study was higher for patients who did not undergo any surgery after presentation compared with patients who did undergo emergency or elective surgery. The majority of patients who died within 30 days (89.5%) had not undergone surgery. The patients' prognosis and quality of life should be taken into account when determining policy and treatment options at the end of life, and surgery should only be performed when essential and when the expected outcome is favorable for the patient.

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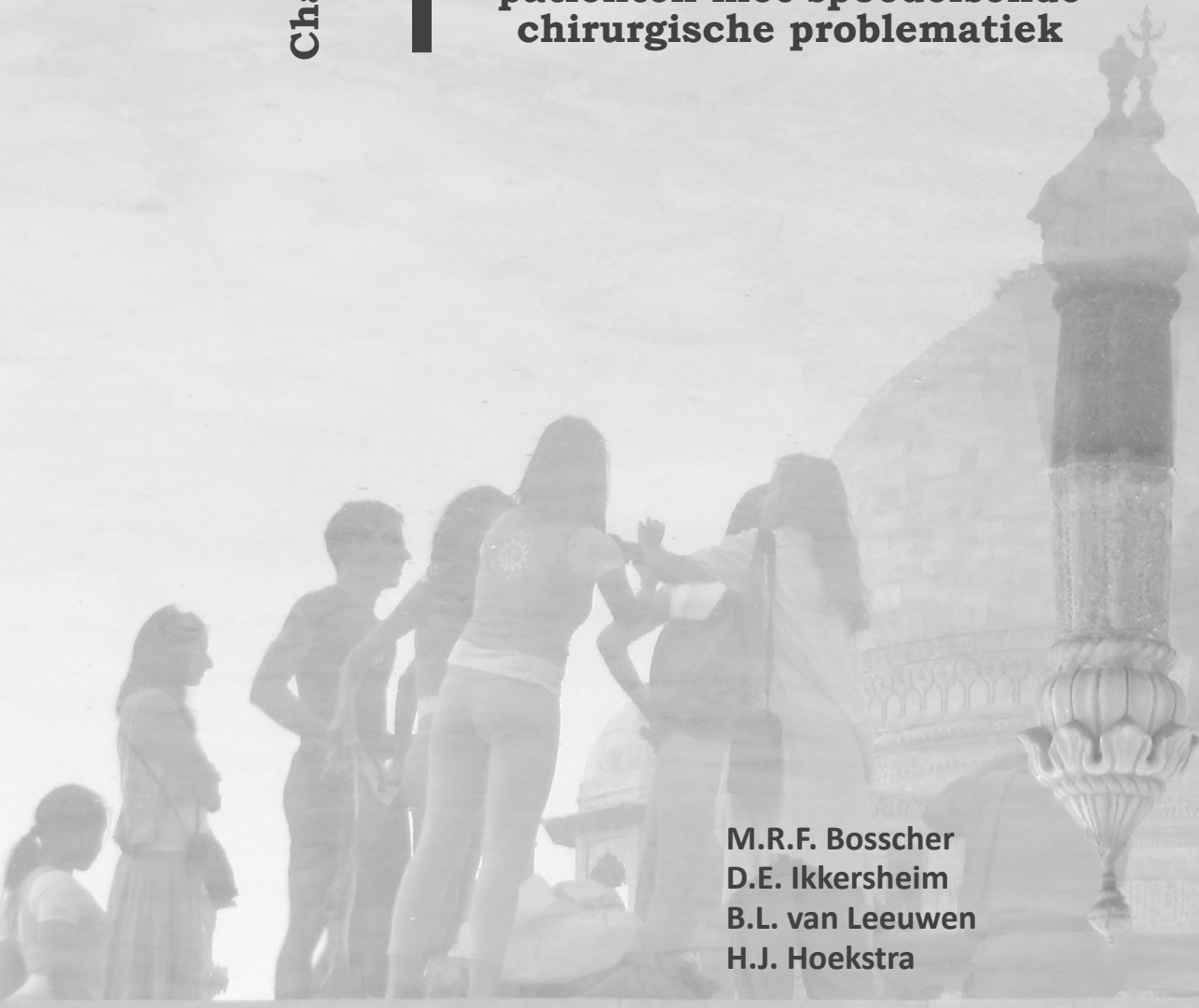
Part II
Current management and clinical outcome of surgical oncologic emergencies

Chapter 4

Kosten van zorg voor oncologische patiënten met spoedeisende chirurgische problematiek



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Costs of care for cancer patients with surgical emergencies

English summary

Introduction

Due to a growing incidence and prevalence of cancer, there will be an increasing number of patients with (a history of) cancer presenting at the Emergency Room (ER). The frequency of ER visits increases near the end of life, and cancer patients admitted through the ER often have advanced malignant disease and poor general prognosis. Some emergency problems require surgical treatment. Examples are gastrointestinal obstruction, perforation, bleeding, infection, and pathological fractures. Making decisions in emergency situations is complex. In an acute setting, it is difficult to gain insight in the prognosis of the physical condition of the patient, and in the outcome of different treatment options. Physicians need to be aware of the occurrence of oncologic emergencies and of the life expectancy of the patients who experience these emergencies. There is no knowledge regarding the outcome and the costs of care for these patients with relatively poor prognosis. The goal of this study was to analyze surgical emergency problems of cancer patients, the provided hospital care and the costs of this care after presentation, plus the subsequent mortality.

Methods

A retrospective chart review was performed of all patients that presented at the ER of the University Medical Center Groningen (UMCG) for surgical oncology consultation between 01-10-2012 and 31-03-2013. All patients with a history of malignant disease were included. Patients were divided into three subgroups: (A) symptoms caused by malignant disease, (B) complications of cancer treatment, and (C) symptoms not related to malignant disease or treatment. Costs of hospital care during the follow up period according to the Dutch health care financial system, and according to the registered intramural interventions were analyzed within the different subgroups.

Results and discussion

A total of 200 patients were included. The 30-day mortality for patients in subgroup A was 25.5% and overall mortality was 62.8%. The median survival of the deceased patients in this subgroup was 69 (0-436) days. The mortality in this subgroup was significantly different compared to the mortality rates of patients in subgroup B or C. The costs of hospital care for patients of subgroup A and who died within 30 days were low (€4.877), and the costs increased along with survival (€27.999 for patients who died between 6 months and 1 year after inclusion, and €47.217 for the patients who died between 1 and 1.5 year). It is a matter of debate what level of expenditures is acceptable for cancer patients with limited life expectancy. The costs of hospital care in the last year of life were higher after presentation at the ER for symptoms caused by malignant disease (subgroup A) or for complications of cancer treatment (subgroup B), compared to the costs of hospital care for patients who presented for other reasons (subgroup C). Furthermore, there were large differences in the costs according to the Dutch health care financial system and the costs based on the intramural interventions. The costs based on the intramural interventions were higher with the largest difference in costs of €34.409 for patients from subgroup A who died between 1 and 1.5 years after inclusion. Apparently, the costs and extent of hospital care for this patient population with limited life expectancy are higher than what would be expected according to the Dutch health care financial system.

Conclusions

This study confirms a high short-term mortality for patients presenting at the ER for symptoms caused by malignant disease. In an emergency situation, estimating the prognosis and outcome of therapies is difficult. The life expectancy, expected outcome, and the costs of care should be taken into account during the decision making process. The costs of hospital care for patients with the shortest survival after presentation at the ER are restricted and increase with longer, yet limited survival. The costs of care according to the Dutch health care financial system are not representative for the real hospital costs for the cancer patients in this study. A multidisciplinary approach and anticipation to the life expectancy could reduce the costs of hospital care and the amount of unbeneficial invasive therapies.

Introductie

Door de toenemende incidentie en prevalentie van kanker neemt het aantal oncologische patiënten dat zich presenteert op de spoedeisende hulp (SEH) toe. Onverwachte progressie van ziekte, een nieuwe vergevorderde maligniteit, of complicaties van (in het verleden) ingestelde therapie kunnen indicaties voor spoedopname zijn [1-4]. De frequentie van SEH-bezoeken neemt toe aan het einde van het leven en patiënten die met spoed worden opgenomen vanwege oncologische problematiek hebben vaak vergevorderde ziekte en een beperkte levensverwachting [2,5-7]. Bij sommige oncologische spoedsituaties is er chirurgische interventie noodzakelijk [8,9]. Voorbeelden hiervan zijn gastro-intestinale obstructie, perforatie, bloeding, infecties en pathologische fracturen.

De besluitvorming in dergelijke situaties is niet eenvoudig. Zowel de oncologische aandoening als het acute probleem beïnvloeden de levensverwachting. De performance status van de patiënt speelt daarnaast een grote rol in het welslagen van een invasieve behandeling. In een acute setting is het vaak moeilijk inzicht te verkrijgen in de specifieke prognose en de uitkomst van verschillende behandelopties.

In 2009 werd 1% van de totale ziekenhuiskosten voor oncologische patiënten in Nederland besteed aan spoedeisende oncologische zorg [10]. Het is van belang dat men zich bewust wordt van de levensverwachting van oncologische patiënten met spoedeisende problemen [11]. Er is momenteel geen goed overzicht van het vóórkomen en de ernst van spoedeisende (chirurgische) problematiek bij oncologische patiënten en ook niet van de uitkomst en de kosten van zorg voor deze patiëntencategorie met een relatief slechte prognose. Het doel van dit retrospectieve onderzoek was inzicht verkrijgen in de chirurgische problematiek waarmee oncologische patiënten zich presenteren op een SEH, de ziekenhuiszorg die verleend wordt na presentatie, de bijbehorende kosten en de mortaliteit op korte termijn.

Methoden

Een retrospectieve analyse werd verricht van volwassen patiënten met een oncologische voorgeschiedenis of actieve oncologische ziekte, die zich tussen 01-10-2012 en 31-03-2013 op de SEH van het Universitair Medisch Centrum Groningen (UMCG) presenteerden voor chirurgisch oncologische consultatie. De follow up eindigde op 31-03-2014.

De patiënten werden in drie groepen verdeeld volgens reden voor presentatie; groep A: symptomen veroorzaakt door oncologische ziekte, groep B: complicaties van oncologische behandeling (chirurgie, radiotherapie, chemotherapie, andere vormen van systeemtherapie) en groep C: klachten niet direct gerelateerd aan oncologische ziekte of behandeling. Aan het einde van de follow up werd in het elektronisch patiënten dossier van het UMCG gekeken of patiënten vrij waren van oncologische ziekte (No Evidence of Disease – NED, AliveWithDisease - AWD) en of ze waren overleden (Death of Disease – DOD, Death Other Causes – DOC). De overleden patiënten werden onderverdeeld in vier categorieën volgens overleving na presentatie.

De geregistreerde DBC's in het UMCG vanaf het moment van presentatie op de SEH tot aan overlijden of het einde van de follow up, met de bijbehorende kosten werden per patiënt geanalyseerd. DBC's die aan het einde van de follow up nog niet waren afgesloten konden niet worden meegenomen in het kostenoverzicht. Vervolgens werd er gekeken naar de absolute ziekenhuiskosten: het aantal geregistreerde verrichtingen in het UMCG vanaf het SEH-bezoek gedurende de follow up en de bijbehorende kosten gebaseerd op de kostprijzen 2012 van de Nederlandse Zorgautoriteit (NZa). Alle data zijn verwerkt met behulp van IBM SPSS statistics 22.

Resultaten

Chirurgische problematiek bij oncologische patiënten en de mortaliteit na presentatie op de SEH

In totaal konden er, uit alle patiënten die in de onderzochte periode de SEH bezochten voor chirurgisch oncologische consultatie, 200 patiënten geïdentificeerd worden met een oncologische voorgeschiedenis of primaire presentatie van oncologische ziekte. De meest voorkomende redenen voor SEH-bezoek waren gastrointestinale obstructieklachten (26,5%) waarvan 41,5% een maligniteit als onderliggende oorzaak hadden. Overige redenen zijn weergegeven in tabel 1.

Tabel 2 geeft een overzicht van de basiskarakteristieken van de patiënten verdeeld in de drie patiëntengroepen volgens reden voor presentatie op de SEH. Na een mediane follow up van 408 dagen waren in totaal 65 patiënten (32,5%) overleden met een mediane overleving van 128 (0-489) dagen. Voor groep A was de 30-dagen mortaliteit 25,5% en de mortaliteit aan het einde van de follow up was 62,8%, met een mediane overleving van 69 (0-436) dagen. De 30-dagen mortaliteit voor patiënten uit groep B en C was 2,8% en 7,1% en de mortaliteit aan het einde van de follow up 20,6% en 26,2% (χ^2 $p<0.001$ voor zowel de 30-dagen, als de algehele mortaliteit tussen groep A en beide andere groepen).

Kosten op basis van reden voor presentatie en overleving na presentatie op de SEH

Tabel 3 geeft een overzicht van de ziekenhuiskosten gedurende de follow up per patiëntengroep, gerelateerd aan de overleving. Bij de patiënten uit groep A waren de ziekenhuiskosten het laagst voor de patiënten met de kortste overleving en werden hoger naarmate de overleving langer was. De hoogste gemiddelde ziekenhuiskosten per overleden patiënt uit deze patiëntencategorie waren op basis van de geregistreerde verrichtingen (de absolute kosten) voor diegenen die overleden tussen 6 maanden en 1 jaar (€27.999), of tussen 1 jaar en 1,5 jaar (€47.217) na presentatie op de SEH. Op basis van de DBC's waren deze kosten een stuk lager (€13.365 en €12.808 respectievelijk).

Tabel 1. Symptomen van oncologische patiënten die zich presenteren op de SEH voor chirurgisch oncologische consultatie

	Totaal **N (%)**	**Groep A** **Veroorzaakt door oncologische ziekte** **N (%)**	**Groep B** **Complicatie van oncologische behandeling** **N (%)**	**Groep C** **Niet gerelateerd aan oncologische ziekte of behandeling** **N (%)**
Totaal	200 (100)	51 (100)	107 (100)	42 (100)
Gastrointestinale obstructie	53 (26,5)	22 (43,1)	21 (19,6)	10 (23,8)
• Benigne	31 (58,5)	-	21 (100)	10 (100)
• Maligne	22 (41,5)	22 (100)	-	-
Wond infecties, abcesvorming, fistelvorming	52 (26,0)	-	45 (42,1)	7 (16,7)
Overige infecties, thrombose	17 (8,5)	-	10 (9,4)	7 (16,7)
Klinische achteruitgang, algehele malaise	17 (8,5)	17 (33,3)	-	-
Gastroenteritis, pancreatitis	15 (7,5)	2 (3,9)	1 (0,9)	12 (28,6)
Problematiek m.b.t. drains, voedingssondes, centraal veneuze lijnen	14 (7,0)	-	13 (12,1)	1 (2,4)
Abdominale sepsis, intestinale perforatie, neutropene enterocolitis	11 (5,5)	1 (2,0)	6 (5,6)	4 (9,5)
Wond- en stomagerelateerde problematiek	8 (4,0)		7 (6,5)	1 (2,4)
Galwegobstructie, cholangitis	8 (4,0)	7 (13,7)	1 (0,9)	-
Bloeding	5 (2,5)	2 (3,9)	3 (2,8)	-

Tabel 2. Karakteristieken van oncologische patiënten die zich presenteren op de SEH voor chirurgisch oncologische consultatie

	Totaal	Groep A Veroorzaakt door oncologische ziekte	Groep B Complicatie van oncologische behandeling	Groep C Niet gerelateerd aan oncologische ziekte of behandeling
Totaal (%)	200 (100)	51 (25,5)	107 (53,5)	42 (21,0)
Mediane leeftijd (jaren)	64 (18–89)	65 (26-84)	63 (18-89)	64 (19-88)
Geslacht				
• Man (%)	109 (54,5)	27 (52,9)	58 (54,2)	24 (57,1)
• Vrouw (%)	91 (45,5)	24 (47,1)	49 (45,8)	18 (42,9)
Spoedopname (%)	114 (57,0)	38 (74,5)	51 (47,7)	25 (59,5)
Mediane duur spoedopname (dagen)	7 (1-71)	10 (1-71)	8 (1-51)	4 (1-26)
Chirurgische spoedinterventie (%)	46 (23,0)	10 (19,6)	24 (22,4)	12 (28,6)
Overleden totaal (%)	65 (32,5)	32 (62,8)	22 (20,6)	11 (26,2)
• < 30 dagen (%)	19 (9,5)	13 (25,5)	3 (2,8)	3 (7,1)
• 30 dagen – 6 maanden (%)	21 (10,5)	12 (23,5)	6 (5,6)	3 (7,1)
• 6 maanden – 1 jaar (%)	15 (7,5)	4 (7,8)	7 (6,5)	4 (9,5)
• 1 jaar – 1,5 jaar (%)	10 (5,0)	3 (5,9)	6 (5,6)	1 (2,4)
Mediane overleving (dagen)	128 (0-489)	69 (0-436)	246 (2-474)	159 (1-489)
Mediane follow up (dagen)	408 (0-547)	196 (0-546)	417 (2-547)	428 (1-541)
Einde follow up of overlijden *				
• AWD/DOD (%)	98 (49,0)	44 (86,3)	37 (34,6)	17 (40,5)
• NED/DOC (%)	91 (45,5)	6 (11,8)	60 (56,1)	25 (59,5)
• Onbekend (%)	11 (5,5)	1 (2,0)	10 (9,3)	-

* AWD: Alive With Disease, DOD: Death Of Disease, NED: No Evidence of Disease, DOC: Death Other Causes

Voor de patiënten uit groep B waren de hoogste gemiddelde absolute ziekenhuiskosten voor de patiënten die overleden tussen 30 dagen en 6 maanden na presentatie op de SEH (€25.411). De gemiddelde kosten op basis van de DBC's waren voor deze patiënten vergelijkbaar (€24.954).

Voor groep C lagen de gemiddelde ziekenhuiskosten over het algemeen lager vergeleken met de andere groepen en werden ook hoger naarmate de overleving langer

was. De verschillen tussen de absolute kosten en de kosten op basis van de DBC's waren voor deze patiëntengroep wisselend. Het grootste verschil tussen de gemiddelde kosten op basis van de DBC's en die op basis van de absolute kosten is te zien voor de patiënten uit groep A die zijn overleden tussen 1 en 1,5 jaar na presentatie op de SEH (een verschil van €34.409).

Beschouwing

Mortaliteit en ziekenhuiskosten na presentatie op de SEH

Zorgbehoeften, geneeskundige kosten en SEH bezoeken nemen toe naarmate het einde van het leven nadert [6,12-16]. Een SEH-bezoek van een oncologische patiënt is vaak een teken van vergevorderde ziekte met een grote kans op overlijden op korte termijn [2,5-7]. Van de patiënten in deze studie die zich op de SEH presenteerden met symptomen veroorzaakt door oncologische ziekte (groep A) overleed 25,5% binnen 30 dagen en 62,8% binnen 1,5 jaar met slechts een mediane overleving van 69 dagen. In deze studie waren de ziekenhuiskosten na het SEH-bezoek voor de patiënten met de slechtste prognose beperkt (slechts €4.877 voor patiënten uit groep A die binnen 30 dagen na presentatie waren overleden) en werden de ziekenhuiskosten logischerwijs hoger naarmate de overleving langer was. Waarschijnlijk is er voor de patiënten met de slechtste prognose in de meeste gevallen een juiste inschatting van de levensverwachting gemaakt, waardoor de kosten voor deze patiënten beperkt zijn gebleven.

Ziekenhuiskosten aan het einde van het leven

Met betrekking tot de waarde van gezondheid vinden Nederlanders gemiddeld dat een Quality-Adjusted Life Year (QALY) € 50.000 mag kosten [17]. In ogenschouw nemend dat de maatschappij dit aanvaardbaar vindt voor levensjaren die doorgebracht worden in volle gezondheid, zou men zich kunnen afvragen wat aanvaardbare kosten zijn voor behandelingen voor (oncologische) patiënten met een beperkte levensverwachting.

Tabel 3. Gemiddelde en mediane totale ziekenhuiskosten in euro per patiënt na presentatie op de SEH o.b.v. DBC/DOT en geregistreerde verrichtingen in het ziekenhuis gerelateerd aan de classificatie voor presentatie en de mortaliteit

		Totale kosten per patiënt o.b.v. DBC/DOT (in Euro's)			Totale kosten per patiënt o.b.v. verrichtingen (in Euro's)		
	N	Gemiddeld	Mediaan	Spreiding	Gemiddeld	Mediaan	Spreiding
Totaal	200	9.608	6.204	(33 - 169.463)	18.343	8.989	(0 - 180.109)
Overleden patiënten	65	9.128	5.017	(64 - 47.535)	15.257	7.398	(0 - 105.859)
• <30 dagen	19	3.082	2.263	(64 - 13.114)	4.259	2.622	(59 - 17.10)
• 30 dagen – 6 maanden	21	12.743	13.256	(1.072 - 47.535)	18.466	9.901	(352 - 98.989)
• 6 maanden – 1 jaar	15	11.921	10.159	(279 - 34.962)	19.607	17.292	(0 - 59.978)
• 1 jaar – 1,5 jaar	10	8.834	4.265	(901 - 23.298)	22.892	13.690	(4.231 - 105.859)
Niet overleden patiënten	135	9.850	7.093	(33 - 169.463)	19.828	9.040	(396 - 180.109)
Groep A Veroorzaakt door oncologische ziekte	51	9.007	6.556	(64 - 31.047)	25.427	10.182	(59 - 180.109)
Overleden patiënten	32	7.690	5.525	(64 - 24.712)	16.897	7.837	(59 - 105.859)
• <30 dagen	13	3.537	3.028	(64 - 13.114)	4.877	2.622	(59 - 17.410)
• 30 dagen – 6 maanden	12	9.017	8.378	(2.627 - 16.561)	18.639	8.703	(1.602 - 98.989)
• 6 maanden – 1 jaar	4	13.365	11.246	(6.255 - 24.712)	27.999	23.542	(4.936 - 59.978)
• 1 jaar – 1,5 jaar	3	12.808	14.226	(901 - 23.298)	47.217	25.946	(9.846 - 105.859)
Niet overleden patiënten	19	11.350	8.641	(148 - 31.047)	39.792	25.870	(1.688 - 180.109)

	N	Totale kosten per patiënt o.b.v. DBC/DOT (in Euro's) Gemiddeld	Mediaan	Spreiding	Totale kosten per patiënt o.b.v. verrichtingen (in Euro's) Gemiddeld	Mediaan	Spreiding
Groep B							
Complicatie van oncologische behandeling	107	11.268	6.737	(33 - 169.463)	17.827	8.391	(0-152.798)
Overleden patiënten	22	13.713	12.934	(199 - 47.535)	15.396	6.999	(0 - 53.415)
• <30 dagen	3	2.111	2.263	(199 - 3.870)	3.646	3.719	(620 - 6.599)
• 30 dagen – 6 maanden	6	24.954	21.175	(13.959 - 47.535)	25.411	25.288	(1.709 - 50.804)
• 6 maanden – 1 jaar	7	14.084	11.991	(279 - 34.962)	15.082	7.398	(0 - 53.415)
• 1 jaar – 1,5 jaar	6	7.839	4.265	(1.185 - 19.720)	11.622	5.914	(4.231 - 30.885)
Niet overleden patiënten	85	10.574	6.727	(33 - 169.463)	18.277	8.470	(560 - 152.798)
Groep C							
Niet gerelateerd aan oncologische ziekte of behandeling	42	6.170	4.574	(148 - 26.583)	11.212	8.196	(352 - 67.943)
Overleden patiënten	11	4.143	3.635	(657 - 13.481)	10.210	9.048	(352 - 35.909)
• <30 dagen	3	2.080	1.949	(657 - 3.635)	2.191	2.068	(1.523 - 2.983)
• 30 dagen – 6 maanden	3	3.226	2.807	(1.072 - 5.799)	3.888	1.410	(352 - 9.901)
• 6 maanden – 1 jaar	4	6.693	4.776	(3.739 - 13.481)	19.134	15.790	(9.048 - 35.909)
• 1 jaar – 1,5 jaar	1	2.878	2.878	-	17.534	17.534	-
Niet overleden patiënten	31	6.873	5.920	(148 - 26.583)	11.845	8.196	(396 - 67.943)

Een analyse van het RIVM laat zien dat in 1999 circa 11% van de totale zorgkosten in Nederland besteed werd aan mensen en kinderen in het laatste jaar van hun leven [12]. Beperkt tot mensen ouder dan 65 jaar was dit zelfs 26,5%. Voor oncologische patiënten (27.9% van alle overledenen) waren de kosten het hoogst: 35.3% van alle kosten voor mensen in het laatste levensjaar en gemiddeld €18.669 per patiënt. De gemiddelde kosten in deze studie lijken vergelijkbaar, maar een belangrijke beperking van deze studie is dat er alleen gekeken is naar de ziekenhuiskosten en niet 1e lijns en/of AWBZ en GGZ kosten. Patiënten krijgen in de laatste fase van hun leven immers vaak ook intensieve zorg buiten het ziekenhuis.

Voor patiënten uit groep A waren de gemiddelde ziekenhuiskosten over een vergelijkbare periode op basis van de geregistreerde verrichtingen bijna twee keer zo hoog (€27.999 voor patiënten overleden tussen 6 maanden en 1 jaar en €47.217 voor patiënten overleden tussen 1 jaar en 1,5 jaar). Voor patiënten uit groep B, die tussen 30 dagen en 6 maanden na presentatie op de SEH zijn overleden, was de periode korter maar de kosten hoger (gemiddeld €25.411). De hoge kosten voor groep B kunnen verklaard worden doordat deze patiënten zich presenteerden met complicaties van oncologische behandeling die gedurende de follow up nog ontvangen werd. Deze kosten, voor zowel groep A als B, zijn gemaakt ondanks een beperkte overleving.

Een opvallende bevinding van deze studie is dat een overzicht van kosten op basis van DBC's niet representatief is voor de werkelijke ziekenhuiskosten en daarmee indirect de intensiteit van ziekenhuiszorg voor oncologische patiënten na het doormaken van een spoedeisend chirurgisch probleem. Er worden grote verschillen gezien tussen de bedragen op basis van de geregistreerde DBC's en die op basis van de geregistreerde verrichtingen in het ziekenhuis (de absolute kosten). De absolute kosten vallen een stuk hoger uit en blijkbaar is de zorg die wordt verleend intensiever dan op basis van een DBC wordt verwacht. De verschillen in bedragen waren voornamelijk groot voor de patiënten uit groep A, de patiëntencategorie met de slechtste prognose en de hoogste mortaliteit. Het grootste verschil in kosten was voor patiënten uit groep A welke overleden tussen 1 en 1,5 jaar na presentatie op de SEH (een verschil van €34.409). Voor deze patiëntenpopulatie met een beperkte overleving, maar welke toch intensieve zorg ontvangt, worden de ziekenhuiskosten niet door een algemene DBC gedekt.

Anticipatie op de levensverwachting

Misschien was het overlijden van de meeste patiënten uit deze studie niet direct te verwachten naar aanleiding van het SEH-bezoek, maar als deze patiënten op dat moment reeds tekenen van progressieve oncologische ziekte hadden, was de levensverwachting al gering. Artsen hebben van nature de neiging om de levensverwachting van (terminale) oncologische patiënten te overschatten [11]. Vooral in een acute situatie kan een inschatting van de prognose en levensverwachting erg lastig zijn. Hiernaast maakt de huidige diversiteit aan behandelopties de besluitvorming betreffende de intentie en intensiteit van zorg in acute situaties niet eenvoudig [18]. Er moet rekening worden gehouden met het effect van een bepaalde ingreep, vooral wanneer de levensverwachting van de patiënt beperkt blijft, ondanks behandeling [17,19]. Wanneer overlijden op korte termijn te verwachten is, zou een optimale kwaliteit van leven de hoogste prioriteit moeten hebben.

Door te anticiperen op de levensverwachting is de kwaliteit van zorg optimaal en blijven zorgkosten (en overbehandeling) beperkt [20]. In 2012 is er in de regio Amsterdam een initiatief gestart genaamd 'Dappere Dokters' [20,21]. Dit initiatief heeft als doel de zorg voor de algemene samenleving te verbeteren door met verschillende disciplines te praten over efficiëntere en goedkopere zorg, overbehandeling te voorkomen en de patiënt centraal te stellen [22]. Voor de (spoedeisende) oncologische zorg zijn deze doelen niet minder belangrijk. Maximale zorg betekent niet altijd optimale zorg. Hogere zorgkosten rondom het levenseinde gaan niet gepaard met een betere overleving en leiden ook niet tot een betere kwaliteit van overlijden [14,20,23]. Door de retrospectieve wijze van deze studie was het helaas niet mogelijk de kwaliteit van leven te meten.

Bij voorkeur gebeurt evaluatie van complexe problematiek altijd in een multidisciplinair overleg (MDO). In een acute situatie is er echter zelden de mogelijkheid voor een "spoed MDO" en worden beslissingen doorgaans gemaakt zonder multidisciplinaire evaluatie [24]. In deze studie hadden de intensiteit van zorg en daarmee de kosten voor een deel van de patiënten mogelijk lager kunnen zijn, wanneer er een (spoed) MDO geweest was. Dan was er een beter inzicht verkregen in de prognose en levensverwachting en had men hier het beleid op kunnen aanpassen.

Artsen moeten te allen tijde een eerlijk gesprek aangaan met de patiënt en familie over de prognose, behandelopties met voor- of nadelen en de verwachte uitkomst van behandeling, ook in de acute situatie. Zo kunnen patiënt en familie een weloverwogen

beslissing nemen over verdere behandeling, of instemmen met het eventueel afzien hiervan [18,25]. Goede communicatie en afspraken over intensiteit van behandeling kunnen leiden tot lagere zorgkosten rondom het levenseinde [14,26]. Patiënten ontvangen minder (onnodige) invasieve behandelingen en overlijden vaker thuis of in een hospice dan op een verpleegafdeling of de Intensive Care [14].

Conclusies

Deze studie bevestigt dat wanneer een patiënt zich presenteert op de SEH met symptomen veroorzaakt door oncologische ziekte, er een grote kans is op korte termijn te overlijden. In een acute situatie is een inschatting van de prognose niet eenvoudig. Tijdens de besluitvorming over de in te stellen behandeling moet men rekening houden met de levensverwachting en het effect en de kosten van een behandeling. Ziekenhuiskosten voor oncologische patiënten met de slechtste prognose na een bezoek aan de SEH zijn beperkt en worden hoger naarmate de overleving langer, maar nog steeds gering is. Een overzicht op basis van DBC's is niet representatief voor de intramurale kosten en intensiteit van zorg voor oncologische patiënten na een SEH-bezoek vanwege spoedeisende chirurgische problematiek. Door te anticiperen op de levensverwachting en ook in de acute situatie voor een multidisciplinaire benadering te kiezen, kunnen kosten en overbehandeling worden beperkt zonder daarbij afbreuk te doen aan de kwaliteit van leven.

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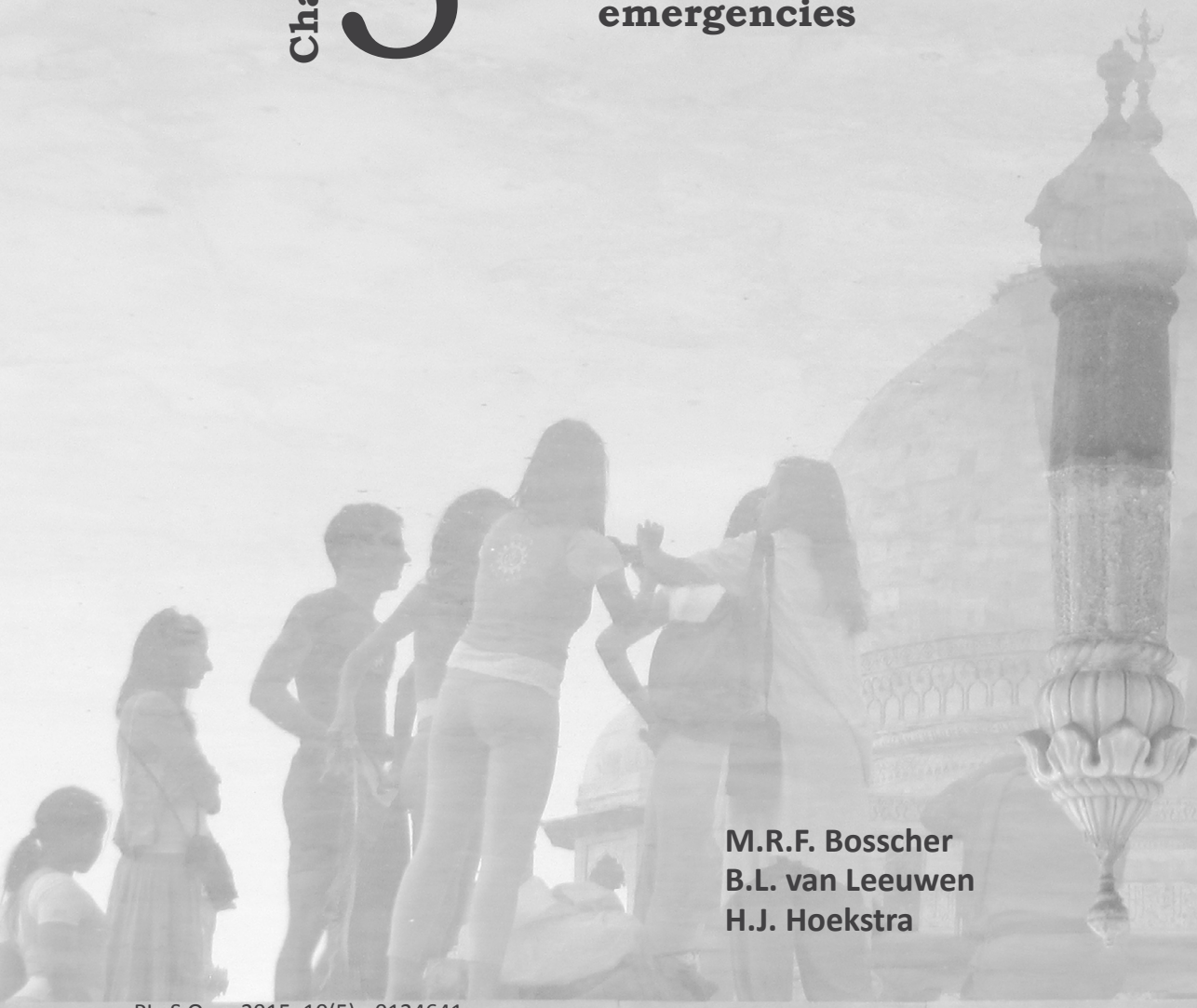
Chapter 5

Current management of surgical oncologic emergencies



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Abstract

Objectives

For some oncologic emergencies, surgical interventions are necessary for dissolution or temporary relieve. In the absence of guidelines, the most optimal method for decision making would be in a multidisciplinary cancer conference (MCC). In an acute setting, the opportunity for multidisciplinary discussion is often not available. In this study, the management and short term outcome of patients after surgical oncologic emergency consultation was analyzed.

Methods

A prospective registration and follow up of adult patients with surgical oncologic emergencies between November 1, 2013 and April 30, 2014. The follow up period was 30 days.

Results

In total, 207 patients with surgical oncologic emergencies were included. Postoperative wound infections, malignant obstruction, and clinical deterioration due to progressive disease were the most frequent conditions for surgical oncologic emergency consultation. During the follow up period, 40% of patients underwent surgery. The median number of involved medical specialties was two. Only 30% of all patients were discussed in a MCC within 30 days after emergency consultation, and only 41% of the patients who underwent surgery were discussed in a MCC. For 79% of these patients, the surgical procedure was performed before the MCC. Mortality within 30 days was 13%.

Conclusions

In most cases, surgery occurred without discussing the patient in a MCC, regardless of the fact that multiple medical specialties were involved in the treatment process. There is a need for prognostic aids and acute oncology pathways with structural multidisciplinary management. These will provide in faster institution of the most appropriate personalized cancer care, and prevent unnecessary investigations or invasive therapy.

Introduction

An oncologic emergency is an acute, potentially life threatening condition that has developed directly or indirectly as a result of cancer or cancer treatment [1, 2]. Non-elective consultation for symptoms caused by malignant disease is an important marker of poor prognosis [3-8]. For some oncologic emergencies, surgical interventions may be necessary for dissolution or temporary relieve [9]. Not all cancer patients will benefit from surgery. A surgical intervention is irreversible, and can result in severe complications. For patients with poor performance and/or advanced disease, invasive treatment could have a detrimental impact on the life expectancy and quality of life.

It is hardly possible to draught guidelines for the management of surgical oncologic emergencies. The great inter-patient variability and an even greater variety of influencing factors require that every patient needs to be evaluated individually [9]. In the absence of these guidelines, the most optimal method for objective evaluation and decision making would be discussion in a multidisciplinary cancer conference (MCC) [10]. It is essential to define the prognosis of both the emergency and the cancer stage, and taking into account the patient's performance score when deciding on the treatment [9, 11]. The most appropriate therapy is the treatment that has clinical benefit, and does not reduce the quality of life. Decisions regarding treatment in emergency situations are often not easy to make, and a multidisciplinary approach can provide in more solid arguments regarding the invasiveness of treatment. In an acute setting, time is scarce and the opportunity for multidisciplinary discussion is often not available. Decisions have to be made timely for prompt management of the emergency, and thus are often made by a single specialist. Acute oncology teams and units have been introduced for the care for patients with oncologic emergencies. These teams could prevent unnecessary investigations or therapy, and can provide in quick referral to palliative care when necessary [12-17]. However, specialized acute oncology care is not widely implemented in common medical practice.

In order to provide arguments for the future development of structural acute oncology pathways for faster institution of optimal care, it is important to be aware of (1) the occurrence of (surgical) oncologic emergencies, (2) the decisional process and the amount of patients being discussed in multidisciplinary cancer conferences, and (3) the clinical

outcome of current management. In this study, the management and short term outcome of patients after surgical oncologic emergency consultation was analyzed.

Materials and Methods

A prospective registration and follow up was performed for adult cancer patients (age > 18) in the University Medical Center Groningen (UMCG), who required consultation for surgical oncologic emergencies, between November 1, 2013 and April 30, 2014. The protocol was consistent with the declaration of Helsinki of 1975, as revised in 1983, and approval for the study was retrieved from the institutional Medical Ethics Committee of the University Medical Center Groningen. Written informed consent was retrieved from participants, and all data were analyzed anonymously.

Criteria for inclusion were: surgical oncologic emergency consultation for symptoms caused by any type of malignant disease (including primary presentation), or for symptoms caused by current or previous cancer treatment (surgery, radiation therapy, chemotherapy, drug targeted therapy). When a surgical oncologist and/or surgical resident was involved in the diagnostic and decisional process, and the possibility of surgical treatment had been evaluated, the consultation was regarded as being a surgical oncologic emergency consultation. Patients who required emergency consultation for symptoms that could not be related to malignant disease or cancer treatment were excluded for analysis. This means that the entire hospital population was studied, including patients who were initially admitted on other than surgical wards (e.g. gynecology, internal medicine) and required surgical oncologic consultation.

Patients who required surgical emergency consultation through four possible pathways were to meet the inclusion criteria: (1) presentation at the Emergency Room (ER), (2) non-elective admission through the (surgical) outpatient clinic, (3) transfer from other hospitals, and (4) in-hospital request of surgical consultation for patients admitted for other specialties.

General patient characteristics were documented upon inclusion; gender, age, oncological history, previous cancer treatment, disease status before the emergency

consultation (not being diagnosed with cancer, Alive With Disease – AWD, No Evidence of Disease – NED - after cancer treatment), intention of the current cancer treatment (diagnostic, curative, palliative). The following variables were documented during the follow up: type of surgical oncologic emergency, type of treatment (i.e. surgical procedures or other interventions), number of involved medical specialties during hospital admission, and whether the patient was discussed in a Multidisciplinary Cancer Conference (MCC). In the UMCG, multiple regularly scheduled MCC's for different cancer types are integrated in common cancer care. In general, they include the disciplines that are involved in the diagnostic process and treatment according to the prevailing guidelines. For this study, a patient was regarded as being discussed in a MCC when a report of the MCC was documented in the patient's chart.

The follow up period was 30 days. At final follow up, the patients' charts were analyzed for disease status (AWD, NED), intention of cancer treatment (curative, palliative) and mortality. All data were processed through IBM SPSS Statistics 22 for statistical analysis.

Results

During the study period, 3737 patients had visited the ER for surgical consultation, and 402 of these patients (11%) had a previous history of cancer, or active malignant disease. After visiting the ER, 147 patients (4% of all 3737 patients, and 37% of the 402 cancer patients) were identified to have surgical oncologic emergencies and were included for analysis. The remaining patients visited the ER for non-oncologic issues. Furthermore, 19 cancer patients were non-electively admitted through the surgical outpatient clinic for surgical oncologic emergencies, another 35 cancer patients required in-hospital surgical oncologic emergency consultation during admission for other medical specialties, and 6 patients were transferred from other hospitals.

Table 1. Baseline characteristics of cancer patients who experienced surgical oncologic emergencies.

	Total (n=207)
Male	101 (48.8)
Female	106 (51.2)
Median Age	64 (19 – 92
ECOG – WHO Performance score	
• 0	57 (27.5)
• 1	85 (41.1)
• 2	47 (22.7)
• 3	14 (6.8)
• 4	4 (1.9)
ASA classification	
• 1	22 (10.6)
• 2	136 (65.7)
• 3	49 (23.7)
Doctors' shift of consultation	
• Day	126 (60.9)
• Evening	24 (11.6)
• Night	11 (5.3)
• Weekend day	26 (12.6)
• Weekend evening/night	20 (9.7)
Route consultation	
• Emergency Room	147 (71.0)
• In-hospital consultation	35 (16.9)
• Outpatient clinic	19 (9.2)
• Transfer from other hospital	6 (2.9)
Time since cancer diagnosis	21 (10.1)
• No cancer diagnosis before emergency consultation	
• <30 days	26 (12.6)
• 30 days – 6 months	56 (27.1)
• 6 months – 1 year	20 (9.7)
• 1 – 2 years	13 (6.3)
• 2 – 5 years	41 (19.8)
• > 5 years	30 (14.5)
Other type of cancer	
• No	174 (84.1)
• Yes	33 (15.9)

	Total (n=207)
Cancer type	
• Colorectal carcinoma	54 (26.1)
• Hepatobiliary	18 (8.7)
• Breast cancer	14 (6.8)
• Soft tissue sarcoma/GIST	14 (6.8)
• Neuroendocrine tumor	13 (6.3)
• Melanoma	11 (5.3)
• Cervix carcinoma	8 (3.9)
• Hematologic malignancy	8 (3.9)
• Esophageal carcinoma	7 (3.4)
• Non-melanoma skin cancer	6 (2.9)
• Lung carcinoma	4 (1.9)
• Prostate carcinoma	3 (1.4)
• Ovarian carcinoma	3 (1.4)
• Gastric carcinoma	2 (1.0)
• Other	7 (3.4)
• Unknown	14 (6.8)
• No cancer	21 (10.1)
Documented stage of treatment before surgical oncologic emergency consultation	
- No cancer	21 (10.2)
- Active disease	129 (62.3)
• Diagnostic stage	32 (15.5)
• Receiving treatment with curative intent	49 (23.7)
• Palliative stage	48 (23.2)
- NED* after being treated for cancer in the past	57 (27.5)
• < 30 days	19 (9.2)
• 30 days – 6 months	10 (4.8)
• 6 months – 1 year	7 (3.4)
• 1-2 years	6 (2.9)
• 2-5 years	6 (2.9)
• > 5 years	9 (4.3)
Previous Radiotherapy	66 (31.9)
Previous Chemotherapy	72 (34.8)
Previous Surgery	126 (60.9)
Time since last cancer treatment	
• Continuously	24 (11.6)
• < 30 days	62 (30.0)
• 30 days – 6 months	32 (15.5)
• 6 months – 1 year	9 (4.3)
• 1 – 2 years	15 (7.2)
• 2 – 5 years	5 (2.4)
• > 5 years	12 (5.8)
• No cancer treatment	48 (23.2)

* NED: No Evidence of Disease

In total, 207 patients with surgical oncologic emergencies were included for analysis through all pathways. There were 101 (49%) males and 106 (51%) females, and median age was 64 (range 19-92) years. Of all patients, 21 patients had a primary presentation of malignant disease, 132 patients were alive with disease (AWD) that was previously diagnosed, and 54 patients had No Evidence of Disease (NED) after being treated for cancer in the past, of whom 9 patients presented with recurrent disease. Of the patients who had been diagnosed with cancer in the past, the most prominent type of cancer was colorectal carcinoma (26%). Table 1 provides an extensive overview of the baseline characteristics for all 207 cancer patients with surgical oncologic emergencies.

Obstruction (e.g. colorectal, biliary, small intestine), and infection were the most frequent conditions for surgical oncologic emergency consultation (42% and 32% respectively) (Table 2).

After surgical oncologic emergency consultation at the ER, 109 of the 147 patients (74%) were directly hospitalized. Four of the remaining 38 patients (11%) had an emergency admission within 30 days after the first consultation at the ER. Together with the patients who were already hospitalized before the surgical oncologic emergency consultation (the patients who required in-hospital consultation or transfer from other hospitals), 173 of all patients with surgical oncologic emergencies (84%) had been hospitalized during the study period.

During hospitalization, the median number of radiologic, endoscopic, and surgical interventions was 1 (range 0 – 09). Eighty three of all patients (40%) underwent surgery during the follow up period. The median duration between inclusion and surgery was 38 hours (range 0 – 720 hours/30 days). Of these patients, 70 patients (84%) underwent surgery in an emergency setting after a median period of 25.5 (range 0 – 720) hours, and 13 patients (16%) underwent elective surgical procedures after a median period of 16 (range 7 – 30) days.

The median number of involved medical specialties during admission was 2 (range 1 – 8). Within 30 days after surgical oncologic emergency consultation, 61 patients (30%) were discussed in a MCC, after a median duration of 12 (range 1 – 30) days. For only 25 of these patients (15% of all hospitalized patients, and 41% of all patients who were discussed), the MCC took place while they were hospitalized after a median period of 8 (range 1 – 35) days after emergency consultation. The remaining 36 patients were discussed in a MCC

after discharge from the ER or hospital ward. Of the 62 patients with symptoms caused by malignant obstruction, 42% were discussed in a MCC (Table 2), and 61% of these patients underwent surgical treatment during the follow up period. Gastrointestinal perforation in the presence of tumor mass (14%), benign obstruction (17%), and postoperative wound infections (20%) were the diagnoses with the lowest rates of multidisciplinary discussion.

Only 34 (41%) of the 83 patients who underwent surgery were discussed in a MCC during the follow up period. For 27 of these 34 patients (79%), the surgical procedure was performed before the MCC, and only 7 patients (21%) were discussed in a MCC prior to surgery. Regarding the moment of surgery in relation to the moment of the MCC, the median period was 9 days prior to (range 26 days prior to – 21 days after) the MCC (Figure 1).

Before surgical oncologic emergency consultation, 32 patients (16%) were in a diagnostic and/or staging process, 49 patients (24%) received cancer treatment with curative intent, 57 patients (28%) had NED after being treated for cancer in the past, and 48 patients (23%) were diagnosed to have incurable malignant disease and were in a palliative stage of treatment. Another 21 patients (10%) had no cancer diagnosis before surgical oncologic emergency consultation, and had a primary presentation of malignant disease. At final follow up, 70 patients (34%) received adjuvant treatment with curative intent or were scheduled for supplementary curative surgical procedures, 42 patients (20%) were NED, and 69 patients (33%) were in a palliative stage, and 26 patients (13%) were deceased.

Many of the patients who were in a palliative stage at final follow up had undergone surgery after inclusion (52%), and 35% of all the patients who were deceased. Most patients died of progressive disease (77%) and 23% died of clinical sepsis or multiple organ failure. Of the deceased patients, 12 (46%) died at home after the institution of palliative care, 10 (39%) died during hospital admission, and 4 patients (15%) were transferred to a nursing home or hospice. Figure 2 visualizes the clinical pathway of the cancer patients in this study.

Table 2. Diagnosis after surgical oncologic emergency consultation and 30 day follow up for surgical interventions, mortality, and discussion in a multidisciplinary cancer conference (MCC) within the follow up period.

Classification	N	Diagnose	N	Surgery	Deceased	MCC*
Obstruction	86	Malignant	62	38 (61.3)	8 (12.9)	26 (41.9)
		• Colorectal	22	16 (72.7)	3 (13.6)	11 (50.0)
		• Biliary	19	7 (36.8)	1 (5.3)	6 (31.6)
		• Small intestine	18	14 (77.8)	4 (22.2)	7 (38.9)
		• Airway	2	1 (50.0)	-	2 (100)
		• Gastroesofageal	1	-	1 (100)	-
		Benign	24	10 (41.7)	1 (4.2)	4 (16.7)
		• Colorectal	8	1 (12.5)	-	1 (12.5)
		• Small intestine	7	5 (71.4)	1 (14.3)	1 (14.3)
		• Radiation enteritis	4	4 (100)	-	1 (25.0)
		• Biliary	3	-	-	1 (33.3)
		• Gastroesofageal	1	-	-	-
		• Urinary	1	-	-	-
Infection	67	Postoperative wound infection	25	3 (12.0)	2 (8.0)	5 (20.0)
		• Score 1 or 2**	6	-	-	-
		• Score 3 or 4	17	2 (11.7)	-	5 (29.4)
		• Score 5	2	1 (50.0)	2 (100)	-
		Infection/neutropenic enterocolitis during chemotherapy	11	4 (36.4)	2 (18.2)	-
		Fistula formation after surgery	7	2 (28.6)	-	-
		Intraabdominal infection after surgery	7	1 (14.2)	-	3 (42.9)
		Infectious tumor mass	5	3 (60.0)	1 (20.0)	3 (60.0)
		Wound healing disturbance after radiation therapy and Surgery	4	1 (25.0)	-	-
		• Score 1 or 2**	3	1 (33.3)	-	-
		• Score 3	1	-	-	-
		Chronic presacral absess formation after pelvic surgery and radiation therapy	3	-	-	1 (33.3)
		Postoperative gastroenteritis	3	-	-	-
		Lymphedema/erysipelas	2	-	-	-
Clinical deterioration	19	Clinical deterioration due to progressive metastatic disease	9	1 (11.1)	4 (44.4)	2 (22.2)
		Clinical deterioration and pain due to progressive tumor mass	8	3 (37.5)	3 (37.5)	4 (50.0)
		Clinical deterioration being NED***	2	-	1 (50.0)	-

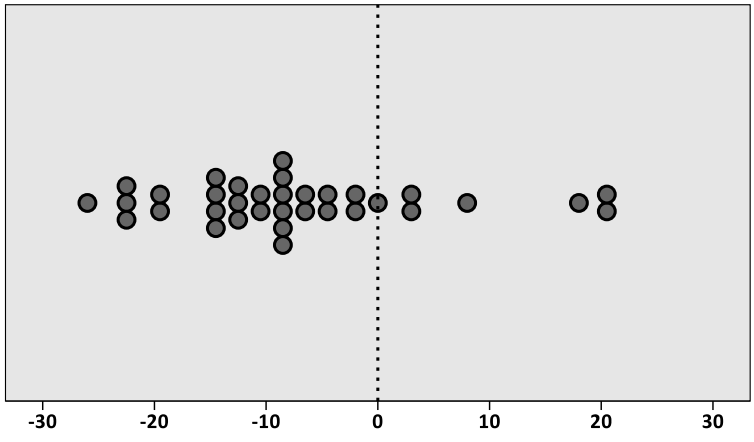
Classification	N	Diagnose	N	Surgery	Deceased	MCC*
Gastrointestinal leak	12	Perforation in the presence of tumor mass	7	6 (85.7)	3 (42.9)	1 (14.3)
		Anastomotic leak after surgery	5	3 (60.0)	-	2 (40.0)
Bleeding/ thrombosis	12	Tumorbleeding	8	2 (25.0)	-	3 (37.5)
		Paraneoplastic arterial/venous thrombosis	3	1 (33.3)	-	1 (33.3)
		Postoperative bleeding	1	1 (100)	-	1 (100)
Pathological fracture	5	Fractures due to bone metastases	5	3 (60.0)	-	1 (20.0)
Other	6	Lymphadenopathy/malignant swelling	3	1 (33.3)	-	1 (33.3)
		Chylus leakage postoperative	2	-	-	1 (50.0)
		Incidental diagnosis on imaging studies	1	-	-	1 (100)

* MCC: Multidisciplinary Cancer Conference

** According to the Southampton Wound Assesment Scale

*** NED: No Evidence of Disease

Figure 1. The timing of surgery in relation to the timing of the Multidisciplinary Cancer Conference (MCC). The MCC is set as timepoint 0.



Discussion

To our knowledge, this is the first extensive analysis of surgical oncologic emergencies and the management in clinical practice. For 37% of the cancer patients who had visited the ER, the surgical consultation at the ER was related to a surgical oncologic emergency. Surgeons will not only be confronted with oncologic emergencies through the ER, but also through the outpatient clinic, and in- or inter-hospital consultation. Almost a third of the patients in this cohort were consultated through other pathways than the ER.

In the past decades, MCCs have become common practice, especially in elective oncology care [18]. Cancer patients represent a complex population and often require treatment from multiple medical specialties. In this study, only 30% of the patients who had been consultated for surgical oncologic emergencies had been discussed in a MCC within 30 days after emergency consultation. This is strikingly low, since the national and institutional guidelines require that every cancer patient is discussed in a MCC to establish general agreement before the start of cancer treatment. For all 33 patients the MCC took place at a regular weekly schedule, and acute multidisciplinary discussion upon admission was not available. This means that for the majority (79%) of the patients who were discussed, emergency treatment was instigated before the MCC; for the 34 patients who underwent surgery and who had been discussed, there was a median period of -9 days in relation to the MCC. The rate of patients being discussed in a MCC was regardless of the amount of medical specialties that were involved during admission (a median of 2 different specialties per patient).

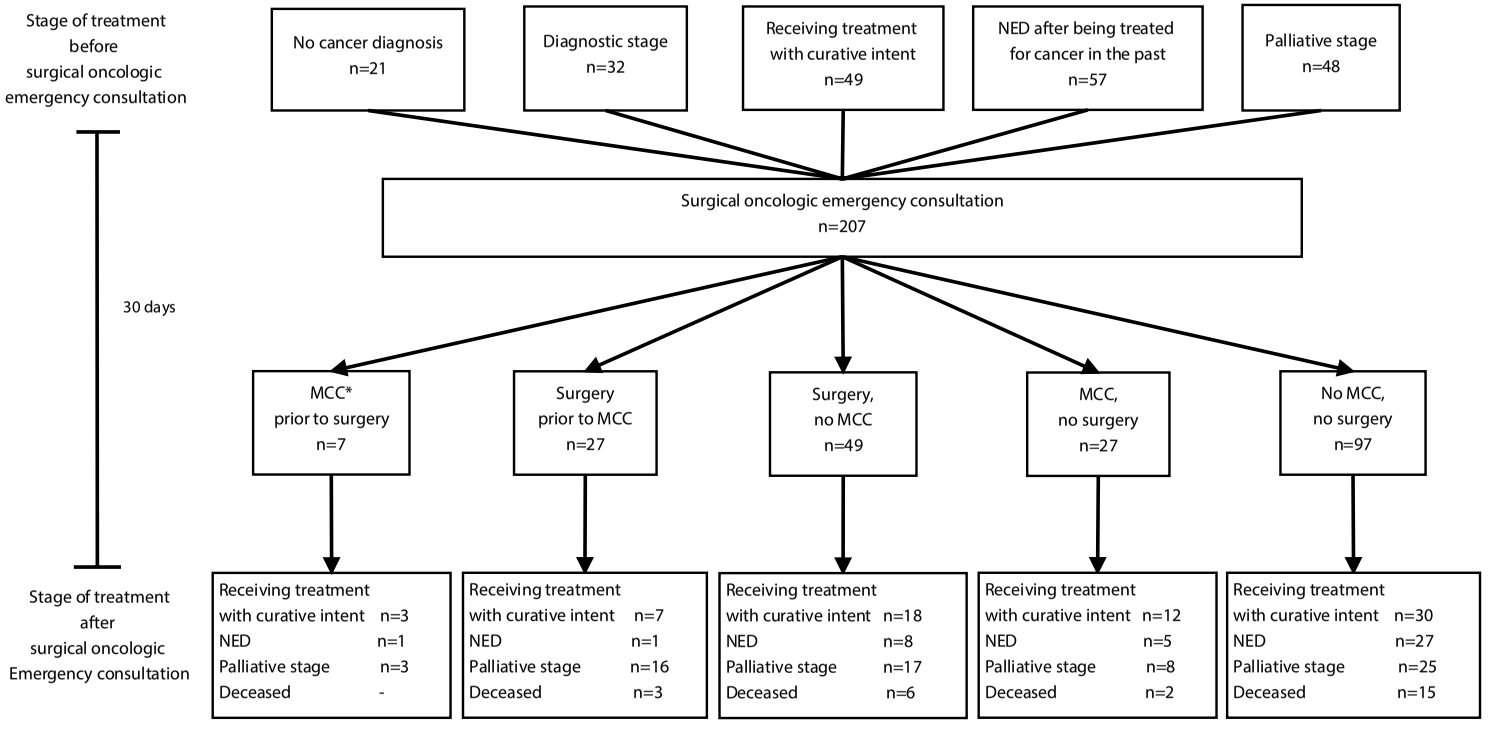
These results confirm the outcome of other studies, that for the most cancer patients who are non-electively treated for surgical oncologic emergencies, emergency (surgical) management - or the decision to refrain from surgery - is performed without discussing the patient in a MCC [10]. Physicians of different medical specialties, who are involved in the treatment process of one patient, can have one-to-one transmissions regarding field specific issues of attention. Nevertheless, without discussing these issues in an organized group-setting, no overall objective view will be obtained in order to connect all issues and transfer these into the same direction of treatment. For patients who require emergency

treatment, - non-scheduled - multidisciplinary evaluation by acute oncology experts should be available.

Obstruction is the most frequent oncologic emergency seen in surgical practice [9]. In this study, of all patients with surgical oncologic emergencies, 42% had symptoms of obstruction with either malignant or benign origin. Surgery often seems to be the best solution for relieve of the obstruction, but could also have an adverse influence on the survival and quality of life. Cancer stage and the performance status of the patient are the most important predictors of survival, and the main factors to influence the successfulness of invasive therapies [11, 19-21]. Patients with obstruction of the gastrointestinal tract often require emergency surgery, and the time frame until the next scheduled MCC will be too large. For all oncologic emergencies, evaluation of all treatment options is essential. Even if the consequences of the emergency are fatally, the quality of life remains the highest priority at the end of life. Only 42% of the 62 patients with symptoms caused by malignant obstruction were discussed in a MCC. However, 61% of all these patients underwent surgical treatment. Gastrointestinal perforation in the presence of tumor mass, benign obstruction, and postoperative wound infections were the diagnoses of patients with the lowest rate of multidisciplinary discussion. The severity of diagnoses (wound infection), and time (gastrointestinal perforation) are possibly factors that have had influence on the different rates of multidisciplinary management.

The number of patients with poor outcome after surgical oncologic emergency consultation was high. Within 30 days, 33% of patients had ended in a palliative stage and 13% were deceased. Taken together, 46% of all patients had poor outcome on very short term. This was twice as many compared to the 23% of patients who were already in a palliative (and thus poor) stage before inclusion. Other studies have reported 30-day mortality rates of 10% and 30% after emergency abdominal surgery in cancer patients [11, 22]. The cohort of patients in this study represents a more heterogeneous category, however, the 30-day mortality rate remains high. Regardless of the outcome, many patients had undergone surgery. Of the patients who ended in a palliative stage, 52% had undergone surgery during the study period, and 35% of all the patients who were deceased.

Figure 2. The 30-day clinical pathway of cancer patients after surgical oncologic emergency consultation. Starting at stage of treatment prior to the consultation, whether patients undergo surgery and/or are being discussed in a *Multidisciplinary Cancer Conference (MCC), and stage of treatment 30 days after surgical oncologic emergency consultation.



* MCC: Multidisciplinary Cancer Conference

Physicians have the tendency to overestimate the life expectancy of terminally ill cancer patients, and it is against the nature of many to spare someone from treatment [23-25]. An earlier study by Ramchandran et al. tried to create a prediction model to identify hospitalized cancer patients at risk for 30-day mortality, based on information only from the electronic medical record [26]. Patients' performance scores were not included in the model, because it requires clinical assessment of the patient. However, the performance score has been reported to be one of the most important predictors of outcome [19-21, 27]. Further research to identify influencing factors, and the development of prognostic tools, is necessary for more accurate prediction of outcome in the acute setting. Prognostic aids for decision making in a multidisciplinary setting will contribute to argumentation for (refraining from) invasive therapies. Further, when the expected outcome of therapies, or a near death, is communicated to the patient and family, it can prevent disappointment after non-successful invasive treatment, and preserve the quality of a patient's life during the last stage [28, 29].

The heterogeneity of the common cancer patient population, and the variety of surgical oncologic emergencies is evident in this study. The interpatient variety (patient performance, cancer stage) is the cause of variable clinical outcome and impedes guidelines for management of these emergencies. This heterogeneity is the core of the difficulties and dilemmas in clinical (surgical) practice, and supports the need for the development of decision aids and acute oncology pathways with structural multidisciplinary management.

Since this is an observational study, it is not possible to evaluate if the treatment of patients with surgical oncologic emergencies would have been different when the decisional process had involved a MCC. The reasons why some patients were discussed in a MCC and others were not is not recorded in this study. For patients who were discussed and underwent surgical procedures, the median time period of 9 days between surgery and a MCC implicates that at this point the MCC's are used for decision making after a pathology result is present, and not for acute treatment decisions including surgery. Furthermore, the fact that, also for many patients who were not discussed in a MCC, multiple medical specialties were involved in the treatment process, could reflect the complexity of pathology.

This study was performed in one tertiary university hospital, and comparison to other hospitals will be difficult. However, since the patient population represents an entire hospital population, the authors believe that the results of the current study reflect

common medical practice. In most hospitals, patients with oncologic emergencies will present through the ER, and specialized acute oncology care has not been implemented in standard emergency care.

The implementation of acute oncology pathways, providing systematic multidisciplinary management of all patients, would be the most optimal way for decision making and treatment of patients with oncologic emergencies [12-17]. Acute oncology care should include structural availability of a specialized team of (at least) an emergency care specialist, a surgical oncologist, a radiation oncologist, a medical oncologist, a palliative care specialist, and an oncology nurse. This team will be trained in acute oncology care, and should be available throughout the day and evening (in exclusive cases during the night). The members of this acute oncology team need to be involved in the evaluation and treatment process directly after emergency presentation. In this way, non-scheduled multidisciplinary decision making will be possible and personalized treatment can be instituted on the shortest term, preventing delay of required therapies or overtreatment. Close involvement of the patient's general practitioner is required during hospital admission. In this way, when invasive treatment is not expected to be favorable for the patient, palliative care can be instituted more efficiently and on shorter term. At the end of life, the length of hospitalization should be limited to only what is needed for care with clinical benefit. Further prospective research is necessary to investigate the influence of acute oncology pathways and structural multidisciplinary management on the clinical outcome and quality of life.

Conclusions

Obstruction (i.e. colorectal, biliary, small intestine) and infection were the most frequent conditions for surgical oncologic emergency consultation. Many patients ended in a palliative stage, and the overall mortality within 30 days was 13%. In most cases, emergency treatment, including invasive therapies such as surgery, occurred without discussing the patient in multidisciplinary cancer conferences, regardless of the fact that multiple medical specialties were involved in the treatment process. There is a need for the development and evaluation

of prognostic aids and acute oncology pathways providing in structural multidisciplinary management. It will result in institution of the most appropriate personalized cancer care on the shortest term, preventing delay of required therapies or overtreatment.

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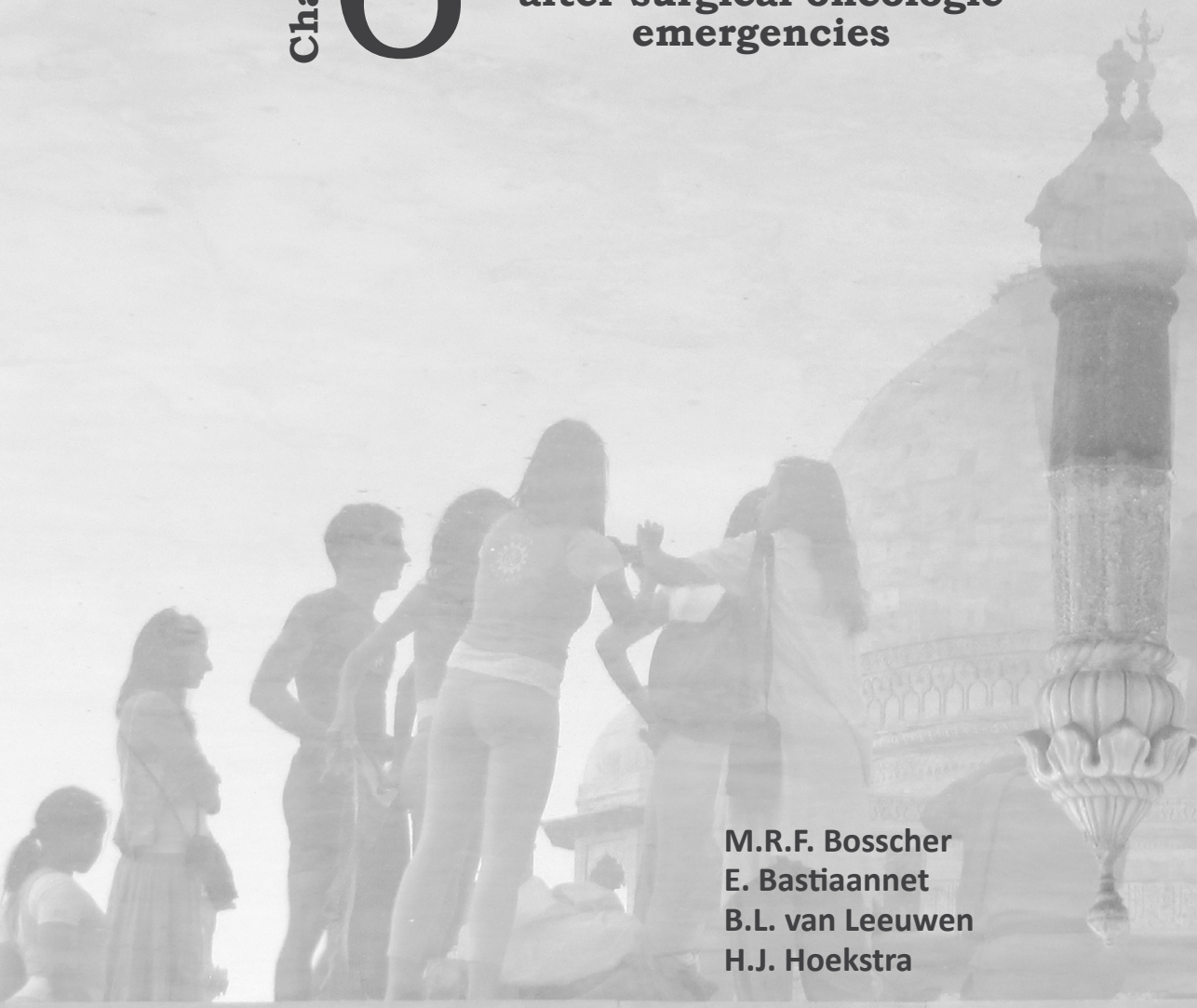
Part III
Survival prediction

Chapter 6

Factors associated with mortality after surgical oncologic emergencies



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Abstract

Purpose

The clinical outcome of patients with oncologic emergencies is often poor and mortality is high. It is important to determine which patients may benefit from invasive treatment, and for whom conservative treatment, and/or palliative care would be appropriate. In this study prognostic factors for clinical outcome are identified, in order to facilitate the decision making process for patients with surgical oncologic emergencies.

Methods

A prospective registration for patients over 18 years of age, who were consulted for surgical oncologic emergencies between November 2013 and April 2014. Multiple variables were registered upon emergency consultation. The follow up period was 90 days. Multivariate logistic regression analysis was performed to identify factors associated with 30-day and 90-day mortality.

Results

During the study period, 207 patients experienced surgical oncologic emergencies. There were 101 (48.8%) men and 106 (51.2%) women; median age was 64 (range 19 - 92) years. The 30-day mortality was 12.6%, 90-day mortality was 21.7%. Factors significantly associated with 30-day mortality were: palliative intent of cancer treatment prior to emergency consultation (p=0.006), ECOG Performance Score (ECOG-PS) of greater than 0 (p for trend: p=0.03), raised LDH (p<0.001). Additional factors associated with 90-day mortality were low handgrip strength (HGS) (p=0.01) and low albumin (p=0.002).

Conclusions

Defining the intent of prior cancer treatment and the ECOG-PS are of prognostic value when deciding on treatment for patients with surgical oncologic emergencies. Additional determination of serum LDH and albumin levels, and measurements of HGS can serve as objective parameters to assess individual prognosis.

Introduction

An oncologic emergency is an acute condition, experienced by a cancer patient, that develops directly, or indirectly from cancer or cancer treatment [1]. Surgical procedures may be necessary as a (temporary) remedy [2]. The clinical outcome of patients with surgical oncologic emergencies is often poor and the short term mortality is high [3-7]. Surgical treatment can have severe complications and diminish end of life quality. It is important to determine which patients may benefit from invasive treatment, and for whom non-invasive treatment or referral to end-of-life care would be appropriate. Unfortunately, patient details are often limited in acute situations [8]. The heterogeneity of cancer patients and surgical emergencies, and the wide range of treatment options cause difficulties in decision making. Physicians often overestimate the remaining length of life of advanced cancer patients [9-11].

Many studies have tried to identify prognostic factors and create prediction models for survival to assist decision making regarding cancer patients with advanced disease [10-16]. Only few studies have focused on emergency situations specifically, and even less studies have focused on surgical decisions in emergency situations [17-24]. The aim of this study was to establish prognostic factors for the clinical outcome of patients with surgical oncologic emergencies, in order to facilitate the decisional process regarding treatment in the acute setting. In this way, (emergency) physicians would be able to identify patients with short life expectancy with a minimal amount of information. For this reason, parameters that do not require complex diagnostic procedures were selected for investigation. Thirty-day and 90-day mortality were chosen as primary and secondary endpoints.

Methods

A prospective registration and follow up was performed for adult cancer patients (age > 18) in the University Medical Center Groningen, who required surgical consultation for oncologic emergencies between November 1st 2013, and April 30th 2014. The protocol was consistent with the declaration of Helsinki, and approval for the study was retrieved from

the institutional Medical Ethics Committee.

Criteria for inclusion were consultation for surgical oncologic emergencies. A surgical oncologic emergency was defined as a symptom related to malignant disease or (previous) cancer treatment, for which non-elective surgical consultation and/or admission was required. Patients who were consulted at the Emergency Room, non-electively admitted through the (surgical) outpatient clinic, transferred from other hospitals, and who required in-hospital surgical consultation when admitted for non-surgical specialties were analyzed to meet inclusion criteria.

Preexistent patient characteristics were documented as parameters for disease and functional status: gender, age, oncological history, previous cancer treatment, disease status before the emergency consultation, intention of last cancer treatment, Body Mass Index (BMI), the American Society of Anesthesiologists (ASA) classification, and the Eastern Cooperative Oncology Group-Performance Score (ECOG-PS). The ECOG-PS has a stronger association with survival when compared to the Karnofsky Performance Status, and provides in better differentiation between ambulatory and bed-ridden patients [25]. The intent of cancer treatment was regarded as palliative when the patient was documented to have incurable malignant disease.

Following admission (within a maximum of 72 hours), parameters as proxies of illness were documented: serum leukocyte count, C-Reactive Protein (CRP), hemoglobin level, thrombocytes, albumin and lactate dehydrogenase (LDH). As a parameter of muscle strength, the average of three consecutive handgrip strength (HGS) measurements of the right and left hand was documented, using the Jamar® Plus+ dynamometer (Sammons Preston, Bolingbrook, IL, USA). The Jamar® dynamometer has been found to be more accurate for HGS in advanced cancer patients compared to other dynamometers [26]. The deviation compared to the normative value for HGS according to age and sex was calculated for each patient, and a combination of both hands was subsequently divided into three categories: Low (≤ -4.2 kg deviation), intermediate (between -4.1 and 1.2 kg deviation), and high (≥ 1.2 kg deviation).

The final diagnoses of all patients were classified into different categories: obstruction, infection, clinical deterioration, gastrointestinal perforation, bleeding/thrombosis, pathological fractures, and other [2]. Wound infections were scored according to the

Southamptom Wound Assessment Scale [27]. Intestinal obstruction with clinical evidence of tumor presence was regarded as malignant obstruction. All other cases of (transient) intestinal obstruction in the absence of signs of disease activity were regarded as benign.

The follow up period was 90 days after inclusion. At final follow up, the patients' charts were analyzed for 30-day and 90-day mortality. All data were processed through IBM SPSS Statistics 22 for statistical analysis. The four categories of diagnoses with the highest 90-day mortality were selected; oneway ANOVA tests, a Kaplan Meier plot and Log Rank tests were performed to compare means of the different parameters and survival within these four different categories. Multivariate logistic regression analysis was performed to identify factors associated with 30-day and 90-day mortality for all patients.

Results

During the study period, 207 patients were included for analysis. There were 101 (48.8%) males and 106 (51.2%) females, and median age was 64 (range 19-92) years. The most prominent type of cancer was colorectal carcinoma (26.1%). Table 1 provides an overview of the baseline characteristics of the 207 patients. Obstruction was the most frequent surgical oncologic emergency (41.6%), followed by infections (32.4%) (Table 2). Of all patients, 40.1% were surgically treated within 30 days after emergency evaluation. The remaining 59.9% of the patients received conservative, non-surgical treatment.

The 30-day mortality for all patients was 12.6%, and was highest for patients who presented with clinical deterioration (42.1%), followed by patients who presented with gastrointestinal leak (25.0%) (Table 2). The 90-day mortality for all patients was 21.7%, and was highest for patients with clinical deterioration (52.6%), followed by patients who presented with obstruction (25.6%). The distribution of mortality was statistically different between the different classifications of diagnoses (p=0.002). Of all patients who died after presenting with obstruction, 54.6% died between 30 and 90 days (Figure 1).

Table 1.Baseline characteristics of cancer patients who required consultation for surgical oncologic emergencies (N=207).

		N	%
Age (years)	≤50	42	20.3
	50-64	68	32.8
	65-74	67	32.4
	75+	30	14.5
Sex	Male	101	48.8
	Female	106	51.2
ECOG Performance Score	0	57	27.5
	1	85	41.1
	2	47	22.7
	3	14	6.8
	4	4	1.9
ASA Classification	1	22	10.6
	2	136	65.7
	3	49	23.7
Handgrip Strength**	Low (≤-4.2)	31	14.9
	Intermediate (-4.1 – 1.2)	32	15.5
	High (≥1.2)	32	15.5
BMI	≤ 19.9	18	8.7
	20.0-24.9	68	32.9
	25.0-29.9	50	24.1
	≥30.0	27	13.0
Cancer type	Colorectal carcinoma	54	26.1
	Hepatobiliary	18	8.7
	Breast cancer	14	6.8
	Soft tissue sarcoma/GIST	14	6.8
	Neuroendocrine tumor	13	6.3
	Melanoma	11	5.3
	Cervix carcinoma	8	3.9
	Hematologic malignancy	8	3.9
	Esophageal carcinoma	7	3.4
	Non-melanoma skin cancer	6	2.9
	Lung carcinoma	4	1.9
	Prostate carcinoma	3	1.4
	Ovarian carcinoma	3	1.4
	Gastric carcinoma	2	1.0
	Other	7	3.4
	Unknown	14	6.8
	No cancer diagnosis	21	10.1

		N	%
Second Cancer Diagnosis	No	174	84.1
	Yes	33	15.9
Time since Cancer Diagnosis	No cancer diagnosis before consultation	21	10.1
	<30 days	26	12.6
	30 days – 6 months	56	27.1
	6 months – 1 year	20	9.7
	1 – 2 years	13	6.3
	2 – 5 years	41	19.8
	> 5 years	30	14.5
Documented Stage of Treatment before Surgical Oncologic Emergency Consultation	No cancer	21	10.1
	Active disease	132	63.8
	• Diagnostic stage	33	15.9
	• Receiving treatment with curative intent	51	24.6
	• Palliative stage	48	23.2
	NED* after being treated for cancer in the past	54	26.1
	• < 30 days	19	9.2
	• 30 days – 6 months	10	4.8
	• 6 months – 1 year	7	3.4
	• 1 – 2 years	6	2.9
	• 2 – 5 years	6	2.9
	• > 5 years	9	4.3
Previous Treatment	**Previous Radiation therapy**	66	31.9
	Previous Chemotherapy	72	34.8
	Previous Surgery	126	60.9
Time since Last Cancer Treatment	Continuously	24	11.6
	< 30 days	62	30.0
	30 days – 6 months	32	15.5
	6 months – 1 year	9	4.3
	1 – 2 years	15	7.2
	2 – 5 years	5	2.4
	> 5 years	12	5.8
	No cancer treatment	48	23.2
Intention of Treatment prior to Emergency Consultation	No cancer	21	10.1
	Diagnostic	32	15.5
	Curative	49	23.7
	Follow-up	57	27.5
	Palliative	48	23.2
Type of Treatment for the Surgical Oncologic Emergency	Surgical	68	32.8
	Conservative	139	67.2

* NED: No Evidence of Disease, ** Based on the deviation of normative values according to age and sex

Table 2. Classification of diagnoses of patients with surgical oncologic emergencies together with the 30-day, and 90-day mortality of patients within the different classifications.

Classification	N	30-day mortality N (%)	90-day mortality N (%)	Diagnose	N
Obstruction	86	10 (11.6)	22 (25.6)	Malignant	62
				• Malignant colorectal obstruction	22
				• Malignant bile duct obstruction	19
				• Malignant small bowel obstruction	18
				• Malignant airway obstruction	2
				• Malignant gastro-esofageal obstruction	1
				Benign	24
				• Benign colorectal obstruction	8
				• Benign small bowel obstruction	7
				• Radiation enteritis	4
				• Benign biliary obstruction	3
				• Benign gastro-esofageal obstruction	1
				• Benign urinary obstruction	1
Infection	67	5 (7.5)	9 (13.4)	Postoperative wound infection, 1 or 2*	6
				Postoperative wound infection, 3 or 4*	17
				Postoperative would infection, 5	2
				Infection/neutropenicenterocolitis during chemotherapy	11
				Fistula formation after surgery	7
				Intraabdominal infection after surgery	7
				Infectious tumor mass	5
				Wound healing disturbance after radiation therapy and Surgery, 1 or 2*	3
				Wound healing disturbance after radiation therapy and Surgery, 3*	1
				Chronic presacralabsess formation after surgery and radiation therapy	3
				Postoperative gastroenteritis	3
				Lymphedema/erysipelas	2
Clinical deterioration	19	8 (42.1)	10 (52.6)	Clinical deterioration due to progressive metastatic disease	9
				Clinical deterioration and pain due to progressive tumor mass	8
				Clinical deterioration being NED	2

Classification	N	30-day mortality N (%)	90-day mortality N (%)	Diagnose	N
Gastrointestinal perforation	12	3 (25.0)	3 (25.0)	Perforation presence of tumor mass Anastomotic leak	7 5
Bleeding/ Thrombosis	12	-	-	Tumorbleeding Paraneoplastic arterial/venous thrombosis Postoperative bleeding	8 3 1
Pathological fracture	5	-	1 (20.0)	Fractures due to bone metastases	5
Other	6	-	-	Lymphadenopathy/malignant swelling Chylus leakage postoperative Incidental diagnosis on imaging studies	3 2 1

* According to the Southamptom Wound Assessment Scale

Figure 1. Kaplan Meier plot for Survival of patients with surgical oncologic emergencies, according to the classification of diagnosis, for the classifications with the highest 90-day mortality.

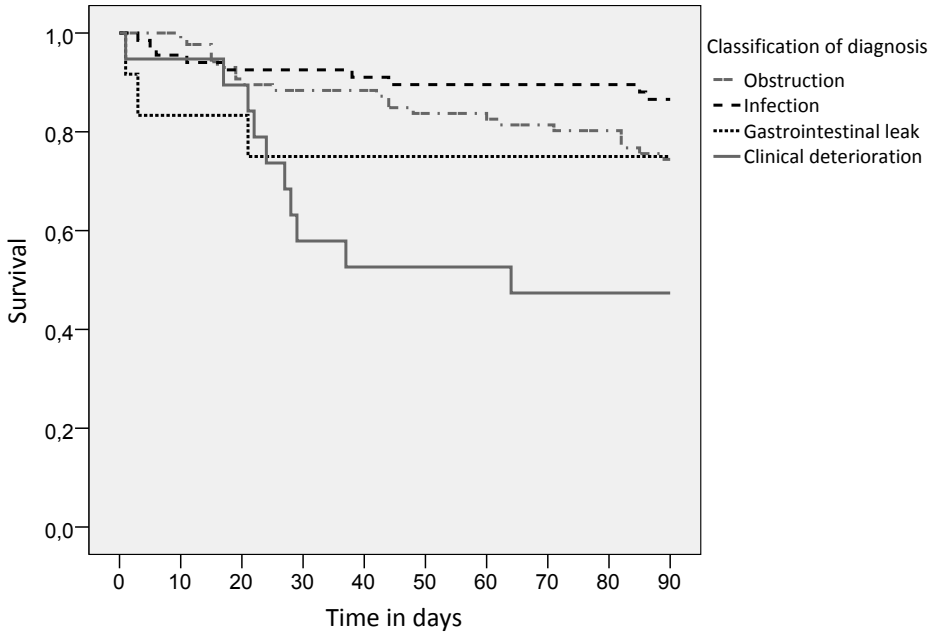


Table 3. The mean values of the different parameters according to the classification of diagnosis, for the classifications with the largest 90-day mortality

Classification		Obstruction	Infection	Clinical deterioration	Gastrointestinal leak	**p value
N (%)		86 (41.6)	67 (32.4)	19 (9.2)	12 (5.8)	
ECOG-PS	Mean	1.21	0.81	2.16	1.17	0.000
	range	0 – 4	0 – 4	1 – 4	0 – 2	
ASA Classification	Mean	2.20	2.01	2.16	2.40	0.068
	range	1 – 3	1 – 3	1 – 3	2 – 3	
CRP	Mean	60	120	47	160	0.000
	range	3 – 420	0 – 432	0 – 308	3 – 385	
Leucocytes	Mean	11.4	11.7	11.5	13.4	0.816
	range	3.9 – 38.8	0.1 – 61.3	5.0 – 19.8	7.4 – 21.9	
Hemoglobine	Mean	7.6	7.1	7.7	7.4	0.152
	range	4.7 – 11.4	3.2 – 10.2	5.7 – 10.0	5.3 – 9.6	
Thrombocytes	Mean	349	306	370	333	0.507
	range	133 – 961	14 – 895	166 – 559	146 – 519	
Creatinine	Mean	86	94	81	87	0.849
	range	29 – 412	35 – 525	24 – 182	36 – 305	
LDH	Mean	210	246	405	214	0.031
	range	0 – 1236	0 – 2180	142 – 1509	122 – 303	
Albumin	Mean	36	33	36	31	0.064
	range	19 – 49	16 – 49	21 – 45	17 – 45	
HGS L*	Mean	-0.3	-4.5	-2.9	-1.8	0.308
	range	-22.6 — 18.6	-18.3 — 3.2	-14.7 — 9.5	-3.7 — 0.2	
HGS R*	Mean	-3.4	-6.9	-7.7	-6.8	0.365
	range	-28.0 — 19.0	-27.4— 12.3	-20.1 — 4.1	-7.6 — -5.6	
BMI	Mean	25.1	26.4	24.6	27.6	0.329
	range	15.4 — 39.0	18.4 — 41.6	17.5 — 32.4	21.5 — 45.9	

*** based on the deviation of the normative according to age and sex**

**** Oneway ANOVA**

Table 3 provides an overview of the mean values of the different parameters that were assessed upon inclusion for the four patient groups with the highest 90-day mortality. The mean ECOG-PS ($p<0.001$), CRP ($p<0.001$), and LDH levels ($p=0.031$) were significantly different between the classifications of diagnoses. Other parameters showed no significant difference. Table 4 shows the results of the uni- and multivariate analysis of the different

variables for 30- and 90-day mortality. Factors significantly associated with 30-day mortality were: palliative intent of treatment prior to emergency consultation (p=0.008), an ECOG-PS greater than 0 (p for trend: p=0.03), and raised LDH (p<0.001). The remaining parameters showed no association with 30-day mortality. Factors significantly associated with 90-day mortality were palliative treatment prior to emergency consultation (p=0.01), ECOG-PS > 0 (p=0.003), low HGS (≤ -4.2 kg deviation of the normative value, p=0.01), raised LDH (p<0.001), and low albumin levels (p=0.002). All these factors remained significant after adjustment for age and sex (Figure 2).

Discussion

In this study, the 30-day mortality for all patients who required consultation for surgical oncologic emergencies was 12.6%, and 90-day mortality was 21.7%. Factors that were significantly associated with 30-day mortality were: Preexistent palliative intent of treatment, an ECOG-PS of greater than 0, and raised LDH. Additionally, low albumin levels and low handgrip strength were associated with 90-day mortality. These factors can all be seen as parameters of decreased functional status (i.e. performance), malnutrition, and/or advanced cancer, which are generally associated with decreased quality of life and survival [28-31].

Advanced cancer (receiving treatment with palliative intent) and raised ECOG-PS (> 0) were significantly associated with 30-day mortality. Although not specifically in an acute setting, the ECOG-PS and other functional status classification systems, have already shown to be correlated with stage of disease, and to be a strong predictor of survival for patients with advanced cancer [10,12,14,22,25,32-34]. In one study, the ECOG-PS was the strongest predictor for mortality for patients with stage IV cancer and malignant bowel obstruction, and the median survival decreased from 222 days to 63 days for patients with an ECOG-PS >1 [22]. These results underscore the importance of defining the cancer stage and functional status of a cancer patient when deciding on treatment, especially in an acute setting. Since time is often scarce, there is a need for objective parameters that could easily be measured, in order to assist in estimating the performance and predicting the clinical outcome of

surgical oncologic emergencies. When patients undergo invasive treatment such as surgery, it is essential that the patient is able to recover from this invasive procedure, and that the procedure itself does not reduce the quality of life.

Blood tests and other laboratory tests are often routinely performed. In this study, raised LDH was significantly associated with 30-day mortality, and low albumin was associated with 90-day mortality after surgical oncologic emergencies. The prognostic value of raised LDH and low albumin for terminally ill cancer has been confirmed by other studies, however it has not been widely investigated in an acute setting [22,25,30,35-37]. The remaining blood markers that were analyzed for this study (i.e. leukocytes, hemoglobin, CRP, thrombocytes, and creatinine), were not generally associated with 30-day mortality or 90-day mortality after surgical oncologic emergencies.

In general, sepsis - often accompanied with elevated serum CRP levels - after emergency surgery is associated with postoperative mortality [38]. In this study, the mortality for patients with high CRP levels was lower compared to patients from other groups. This is possibly due to the fact that most patients within the group of infections had postoperative wound infections, which are often conservatively treated with antibiotics or drainage. Furthermore, the number of patients with severe sepsis was relatively small. Studies on electively treated cancer patients found that CRP is associated with malignant potential and tumor stage, and thus general prognosis [32,39,40]. CRP has been found to increase significantly 1-2 weeks prior to death [41]. In a study evaluating CRP levels in patients with advanced cancer visiting the ER, CRP was considered to be an independent predictor for 14-day mortality, but the specific diagnoses and effect of antimicrobial treatment were not specified [23].

In the present study, low HGS (≤ -4.2 kg deviation of the normative value) was associated with 90-day mortality. HGS has been found be a measure of muscle function, cachexia and malnutrition in several cancer populations, and a better predictor of clinical outcome than measuring the appendicular muscle mass [28,31,42-48]. HGS has been associated with a significantly lower BMI, hemoglobin, and albumin, and increased ECOG-PS. Malnutrition and low HGS have further been associated with an increased length of hospital stay and mortality. In one study, patients with a decline of HGS to less than a 10th percentile of normative values had statistically shorter survival compared to patients with higher HGS, independent of age, gender, oncological treatment, and cancer type [28,43]. Nevertheless, HGS

less than a 10th percentile of the normative value is an extensive decline in strength, and the survival period was relatively long. The current study has found that even a smaller decline in HGS (≤ -4.2 kg deviation of the normative value) was already associated with 90-day mortality.

The results of previous studies and the current study confirm that HGS can be seen as a measurement of functional status, and that low HGS is associated with poor clinical outcome. To our knowledge, this is the first study that evaluated the clinical value of handgrip strength specifically for patients who are consulted for surgical oncologic emergencies. Early measurement of HGS in patients with surgical oncologic emergencies can be of value in order to identify patients with advanced cancer and poor functional status who require referral to palliative care. When dynamometers will become generally available at the Emergency Room and hospital wards, HGS could be an easy measure for patients who require prompt decisions. Unfortunately, the HGS could not be measured prior to treatment in every patient. Many patients were admitted and treated outside office hours when research personnel were not available. Possibly, when more HGS-measurements would have been performed, a stronger association with mortality may have been found.

Clinical functional status scoring systems and other parameters have already been incorporated in multiple prediction models for survival of terminally ill cancer patients [10,25,36,49]. However, none of these models have been evaluated for patients with (surgical) oncologic emergencies. The results of this study confirm that defining the ECOG-PS and cancer stage, measurements of LDH, albumin, and HGS are of prognostic value for patients with surgical oncologic emergencies with respect of 30- and 90-day mortality. When deciding on the extent of treatment, the main goal of treatment should be (temporary) solution of the emergency, without reducing survival or quality of life. Being able to recognize patients who are at the end of life, could prevent unnecessary investigations, expensive treatment, and preserve overall patient satisfaction. The prognostic factors found in this study can supplement the clinical judgment of a physician who is confronted with surgical oncologic emergencies.

Table 4. Factors associated with 30-day and 90-day mortality after surgical oncologic emergencies

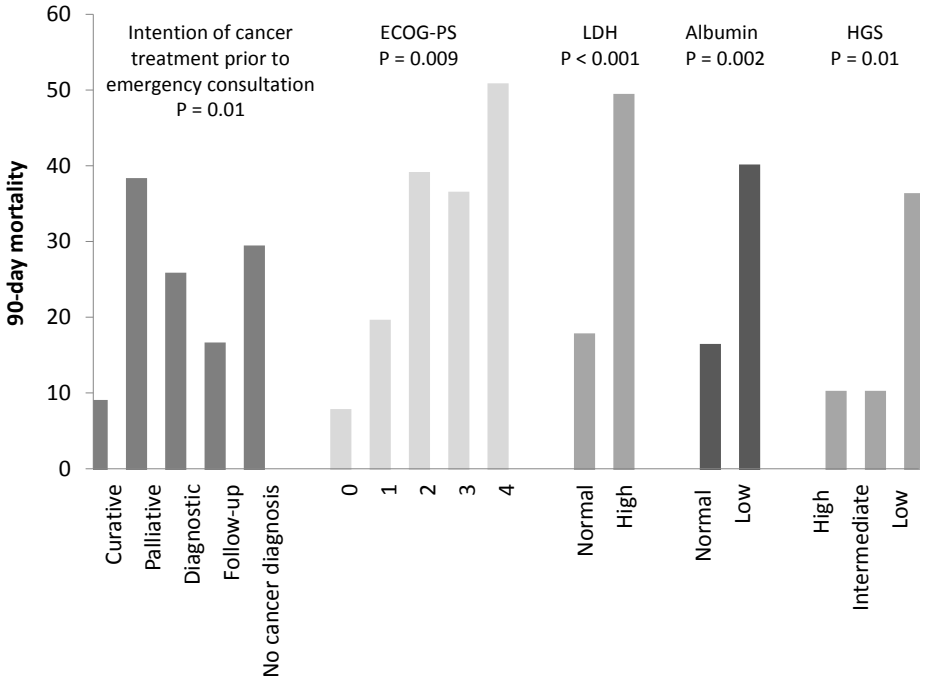
Factor		† 30 days	OR (95%CI)	p	Multivariable OR (95%CI) *	p	† 90 days	OR (95%CI)	p	Multivariable OR (95%CI)*	p
Age**	≤50	9.5	1.0 (ref)	0.5			16.7	1.0 (ref)	0.2		
	50-64	8.8	0.9 (0.2-3.5)				20.6	1.3 (0.5-3.5)			
	65-74	16.4	1.9 (0.6-6.3)				19.4	1.2 (0.4-3.3)			
	75+	16.7	1.9 (0.5-7.8)				36.7	2.9 (1.0-8.7)			
Sex	Male	13.9	1.0 (ref)	0.6			23.8	1.0 (ref)	0.5		
	Female	11.3	0.8 (0.3-1.8)				19.8	0.8 (0.4-1.5)			
ECOG-PS	0	1.8	1.0 (ref)	0.03	1.0 (ref)	0.03	7.0	1.0 (ref)	0.003	1.0 (ref)	0.009
	1	11.8	7.5 (0.9-60.0)		7.0 (0.8-59.1)		18.8	3.1 (1.0-9.7)		3.2 (1.0-10.7)	
	2	21.3	15.1 (1.9-123)		14.3 (1.6-125)		38.3	8.2 (2.5-26.6)		7.9 (2.3-27.8)	
	3	21.4	15.3 (1.5-160)		17.3 (1.5-203)		35.7	7.4 (1.6-32.7)		6.6 (1.3-32.2)	
	4	50.0	56.0 (3.4-906)		59.0 (3.5-985)		50.0	13.2 (1.4-120)		13.7 (1.5-126)	
ASA Classification	1	4.6	1.0 (ref)	0.4			4.6	1.0 (ref)	0.1		
	2	12.5	3.0 (0.4-23.8)				22.1	5.9 (0.8-46.0)			
	3	16.3	4.1 (0.5-34.9)				28.6	8.4 (1.0-68.5)			
Handgrip Strength	High	6.3	1.0 (ref)	0.4			9.4	1.0 (ref)	0.01	1.0 (ref)	0.01
	Intermediate	3.1	0.5 (0.04-5.6)				9.4	1.0 (0.2-5.4)		1.2 (0.2-7.0)	
	Low	12.9	2.2 (0.4-13.1)				35.5	5.3 (1.3-21.5)		6.9 (1.6-29.4)	
BMI	Normal	10.3	1.0 (ref)	0.4			23.5	1.0 (ref)	0.4		
	Low	5.6	0.5 (0.1-4.4)				16.7	0.7 (0.2-2.5)			
	Overweight	6.0	0.6 (0.1-2.3)				12.0	0.4 (0.2-1.2)			
	Obese	18.5	2.0 (0.6-6.9)				22.2	0.9 (0.3-2.7)			

Factor		† 30 days	OR (95%CI)	p	Multivariable OR (95%CI) *	p	† 90 days	OR (95%CI)	p	Multivariable OR (95%CI)*	p
Intention of Treatment prior to Emergency Consultation	Curative	4.1	1.0 (ref)	0.008	1.0 (ref)	0.006	8.2	1.0 (ref)	0.01	1.0 (ref)	0.01
	Palliative	29.2	9.7 (2.1-45.4)		9.8 (2.0-47.2)		37.5	6.8 (2.1-21.9)		6.8 (2.0-22.6)	
	Diagnostic	9.4	2.4 (0.4-15.4)		2.3 (0.4-15.1)		25.0	3.8 (1.0-13.7)		3.6 (1.0-13.5)	
	Follow-up	8.8	2.3 (0.4-12.2)		1.9 (0.3-11.0)		15.8	2.1 (0.6-7.3)		1.9 (0.5-6.8)	
	No cancer	9.5	2.5 (0.3-18.9)		2.0 (0.2-15.7)		28.6	4.5 (1.1-18.1)		3.4 (0.8-14.3)	
Leucocytes	Normal	12.5	1.0 (ref)	0.9			21.3	1.0 (ref)	0.9		
	Low	12.5	1.0 (0.1-9.0)				25.0	1.2 (0.2-6.7)			
	High	13.5	1.1 (0.5-2.6)				23.1	1.1 (0.6-2.2)			
Hemoglobin	Normal	12.5	1.0 (ref)	0.9			18.7	1.0 (ref)	0.4		
	Low	13.3	1.1 (0.4-2.6)				24.2	1.4 (0.6-2.9)			
CRP	Normal	12.5	1.0 (ref)	0.8			12.5	1.0 (ref)	0.1		
	High	13.8	1.1 (0.4-3.5)				24.5	2.3 (0.7-6.9)			
Thrombocytes	Normal	11.7	1.0 (ref)	0.3			20.7	1.0 (ref)	0.3		
	High	17.4	1.6 (0.7-3.7)				27.5	1.5 (0.7-2.9)			
Creatinine	Normal	13.0	1.0 (ref)	0.7			22.7	1.0 (ref)	0.8		
	High	15.2	1.2 (0.4-3.5)				24.2	1.1 (0.5-2.6)			
LDH	Normal	8.2	1.0 (ref)	<0.001	1.0 (ref)	<0.001	17.0	1.0 (ref)	<0.001	1.0 (ref)	<0.001
	High	35.1	6.1 (2.5-14.9)		6.2 (2.5-15.3)		48.6	4.6 (2.1-10.0)		4.8 (2.2-10.6)	
Albumin	Normal	10.4	1.0 (ref)	0.08	1.0 (ref)	0.06	15.6	1.0 (ref)	0.002	1.0 (ref)	0.002
	Low	21.3	2.3 (0.9-6.1)		2.6 (1.0-6.8)		39.3	3.5 (1.6-7.8)		3.9 (1.7-9.0)	

*Age and sex adjusted OR

**Age continue: OR 1.03 (0.99-1.05; p=0.065

Figure 2. Factors associated with 90-day mortality (p-values adjusted for sex and age).



Only two other study have investigated factors associated with mortality in patients with surgical oncologic emergencies [17,24]. Dumont et al. created a preoperative normogram for decision making in surgical oncologic emergencies, which included the ECOG-PS and albumin level (both confirmed by the current study), and the Portsmouth Physiological and Operative Severity Score for the enumeration of Mortality and Morbidity (P-POSSUM) [17].

The major drawback of the P-POSSUM is that this score is not designed for the acute setting and requires comprehensive preoperative diagnostic studies. A study by Roses et al. has identified ASA classification of > 3 and albumin as independent predictors for 30-day mortality [24]. Active malignant disease, a tumor related emergency, ASA > 3, and raised creatinine were independent predictors of decreased overall survival. For the patients in the current study, the preexistent ASA classification was assessed and did not include any patient classified higher than 3. The ASA classification was not associated with short term mortality. The ECOG-PS seems to be a better indicator for clinical outcome.

The cohort of patients in this study represents a very heterogeneous population, and patients experienced a wide range of emergencies with various severities. As this was an observational study, patients were not selected or randomized for invasive or non-invasive treatment according to the prognostic factors. The treatment instituted for each patient was dependent on the decisions of the physicians involved during admission, and was not influenced by this study. Furthermore, the number of patients in the subgroups of this cohort was not large enough to create a solid prediction model. For this reason only factors that were associated with 30-day and 90-day mortality are shown.

Conclusions

Consultation for surgical oncologic emergencies can be a sign of advanced disease, and outcome is often poor. Being able to recognize patients who are at the end of life would prevent unnecessary investigations, expensive treatment, and preserve patient satisfaction. There is a need for parameters that could easily be measured, in order to assist in predicting the clinical outcome. Defining the intention of prior cancer treatment and the ECOG-PS are of prognostic value when deciding on the extent of treatment for patients with surgical oncologic emergencies. Additional measurements of LDH and albumin levels, and HGS can serve as objective parameters to assist the clinical assessment of individual prognosis.

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Chapter 7

Summary and conclusions

Surgical oncologic emergencies
Decision making and clinical outcome

Acute, potentially life threatening conditions that have developed directly, or indirectly, as a result of malignant disease or cancer treatment, are regarded as oncologic emergencies [1,2]. The majority of these conditions require non-elective treatment, and sometimes emergency surgical procedures may be necessary as a remedy or temporary relief [3,4]. In this thesis, the current care for patients with surgical oncologic emergencies is described, as well as the clinical outcome of treatment for this category of patients. This study has been performed to raise the awareness regarding the rate of occurrence of surgical oncologic emergencies, the extent of current hospital care, and the clinical consequences for the patients who experience these emergencies. Furthermore, patient characteristics and parameters have been investigated, which could possibly assist in timely recognition of cancer patients who are at the end of life, and for whom surgical treatment should be renounced.

In *Chapter 1*, the rationale behind this thesis was outlined. Certain surgical oncologic emergencies are signs of advanced, end-stage malignant disease. In non-elective situations, the clinical management and extent of treatment that is instigated often depends on the personal decisions of a single attending physician. These initial treatment decisions can have great impact on the clinical course and the final outcome of treatment. It is important to take into account the patient's individual prognosis and quality of life, before commencing any treatment for the acute problem. Every medical procedure has its consequences, and some procedures may have even more severe complications than the illness itself. Patients need to be physically able to recover from the emergency, but also from the therapies that are instigated for this emergency. For this reason, patients should only undergo invasive procedures when beneficial results are to be expected [5]. In an acute setting also, physicians need to be bold in waiving certain therapies when it does not seem to be advantageous for the patient. A structural multidisciplinary approach, for example with a team of physicians who are specialized in oncologic emergencies, would optimize the decision making. It will result in a more efficient process, and timely instigation of palliative treatment. At the end of this chapter the different topics in this thesis were discussed, all of which can serve

as arguments for the need for improvement of care for patients who experience surgical oncologic emergencies.

Definition and occurrence of surgical oncologic emergencies

There are various surgical emergencies that can occur in cancer patients, and these can have either benign or malignant origin. In *Chapter 2* a summary was given of surgical emergencies that can be experienced by cancer patients. Subsequently, the best approaches and therapeutic options for these emergencies were described. A frequently occurring emergency is gastrointestinal obstruction, but obstruction can also develop in other organs and structures. Examples of which are the urinary tract, the airways, and central nervous system. Other types of surgical emergencies include perforation of the gastrointestinal tract, bleeding events, infectious complications of cancer treatment, and pathological fractures. During the decision making, information on the patient's performance status, cancer stage and prognosis, and the type and severity of the emergency are essential to achieve optimal patient management. The complications of the oncologic emergency can be more life threatening than the intervention, whereas for others the intervention itself can cause a worse outcome and even shorten survival. The type of treatment that should be administered, surgical or conservative, will differ for each single patient.

It is essential to raise the awareness regarding the rate of occurrence of surgical oncologic emergencies in clinical practice and regarding the clinical consequences. In *Chapter 3* the reasons of cancer patients for visiting the emergency room (ER) for surgical oncologic consultation were evaluated through a retrospective analysis. Furthermore, the subsequent mortality after visiting the ER was analyzed. Of all cancer patients who presented at the ER for surgical consultation during a period of six months, 53.5% suffered complications of cancer treatment. Another 25.5% presented with symptoms caused by malignant disease, and only 21.0% showed symptoms that could not be related to malignant disease or cancer treatment. Intestinal obstruction was the most frequent reason for patients to present at the ER. More than one third of obstruction symptoms (41.5%) proved to be malignant of origin. The subsequent mortality was highest for patients who presented at the ER with

symptoms caused by malignant disease. During the follow-up period, 62.8% of all patients from this category died after a median period of 69 days. More than one-third of the deceased patients from this category died within the first 30 days after visiting the ER. Given the high mortality rate and short survival period after ER-visits for symptoms caused by malignant disease, it is essential to consider which intention of treatment will be meaningful for cancer patients at the ER. The mortality after visiting the ER was higher for patients who were excluded for any surgery after presentation, compared with patients who did undergo emergency or elective surgery. The majority of patients who died within 30 days (89.5 % of the deceased patients) had not undergone surgery. Possibly, this could have been the result of the poor physical condition of patients in the acute setting, due to which treatment was waived when no beneficial effect was to be expected.

Current management and clinical outcome of surgical oncologic emergencies

In an emergency situation, estimating the prognosis and outcome of therapies is a serious problem. Visiting the ER for surgical oncologic emergencies can be a sign of advanced disease with short life expectancy. Not only the physical condition of the patient and the life expectancy, but also the expected outcome and the costs of care should be taken into account during the decision making process. *Chapter 4* reviewed the hospital costs for cancer patients after they had visited the ER for surgical consultation, related to the mortality after this visit. This chapter showed that for patients who presented with symptoms caused by malignant disease and who died within 30 days after presentation, the costs of hospital care were restricted to only €4,877. These costs increased with longer, but still limited survival; €27,999 for patients who were deceased between 6 months and 1 year, and €47,217 for patients who were deceased between 1 and 1.5 years. Taking into account that in the Netherlands a Quality Adjusted Life Year is equal to €50,000, one can question what reasonable costs would be for patients with limited life expectancy [6]. Another finding in this chapter was that the costs according to the current Dutch health care financial system did not represent the intramural costs and intensity of care for cancer patients after

visiting the ER for surgical oncologic emergencies. There were large differences between the costs based on the Dutch health care financial system and the costs based on the registered intramural interventions. In general, the latter were higher. Apparently, the costs and extent of hospital care were beyond that what is expected according to the Dutch health care financial system. Mainly, the differences in costs were largest for patients who presented with symptoms caused by malignant disease; the patient category with the worst prognosis and the highest mortality. It is not always possible to predict the death of a patient following an ER-visit, but the prognosis will be poor when patients already show signs of progressive malignant disease. By taking the life expectancy into account, costs of hospital care and unbeneficial invasive therapies can be reduced while preserving the quality of life. When death is expected in the near future, an optimal quality of life should have the highest priority. Maximal care does not always mean optimal care. High costs of care at the end of life do not lead to better survival or an improved quality of life [7-9].

Cancer patients often receive treatment from multiple medical disciplines. An optimal way of making medical decisions in complex (oncologic) situations, is through a communal approach. Therefore, most oncologic clinical guidelines advise to have diagnostic interventions, treatment and follow-up coordinated by a multidisciplinary team. In acute situations however, multidisciplinary discussion is often not available, and important decisions regarding invasive treatment are often made by a single physician. *Chapter 5* analyzed whether patients with surgical oncologic emergencies were discussed in a multidisciplinary cancer conference (MCC), and whether they underwent surgical treatment. Additionally, the clinical consequences for these patients after a period of 30 days were investigated. During the follow-up period, 40% of all patients had undergone surgical treatment after a median period of 38 hours after inclusion. The main part of these surgical procedures (84%) were non-elective. This chapter further showed that in most cases, non-elective invasive therapies such as surgery, were performed without discussing the patient's condition in a multidisciplinary cancer conference. Only 30% of patients were multidisciplinary discussed after a median period of 12 days after emergency presentation, even though multiple medical specialties were involved during hospital admission. Of all patients who underwent surgical treatment, 41% had been discussed in a MCC. However, for most patients (79%), the MCC took place just after the surgical procedure. Therefore, the process of care for these patients with surgical oncologic emergencies did not meet general oncologic guidelines [10-13]. Many patients who experienced surgical oncologic emergencies were already diagnosed

with disseminated disease prior to inclusion, or appeared to have disseminated disease during the short period of follow-up. The overall mortality within 30 days for all patients who experienced surgical oncologic emergencies was 12.6%. At final follow-up, almost half of all patients (46%) was in a palliative stage or deceased. The chapter underscored the need for the development and evaluation of acute oncology pathways, which provide in structural multidisciplinary management in emergency situations, preferably involving the patients' own general practitioners [14]. This would result in faster institution of the most appropriate personalized cancer care, and could prevent unnecessary diagnostics or invasive therapy at the end of life.

Survival prediction

The development of surgical oncologic emergencies can be a sign of advanced disease, and the clinical outcome is often unfavorable for the patient. Being able to timely recognize patients who are at the end of life, could prevent unnecessary and burdensome investigations or treatment, and preserve the quality of life [8,15-17]. In certain emergency situations, quick action may be required. Information regarding recent cancer stage and the functional status prior to admission is mostly incomplete or outdated. There is a need for parameters that could easily be measured, in order to assist in estimating the prognosis and physical condition of the patient, and to gain insight in the clinical outcome of the emergency and possible therapy. In *Chapter 6*, multiple patient characteristics were evaluated for association with short term mortality after surgical oncologic emergencies. The chapter showed that defining the intention of prior cancer treatment and the performance score can be useful information for predicting the clinical outcome. These data can serve as argumentation when decisions must be made on the extent of emergency treatment. In the acute setting, when a patient is severely ill, estimating the performance score of a patient is difficult. Furthermore, information regarding the medical history of the patient may be concise. When solid arguments to renounce therapies are lacking, many physicians tend to provide extensive care. In this chapter, additional parameters were investigated for prognostic value after surgical oncologic emergencies. A High serum LDH and low

albumin levels, and low handgrip strength (HGS) appeared to be associated with short term mortality. On that account, these specific parameters can assist in the (objective) clinical assessment of individual prognosis in acute situations. In this way, personalized treatment can be instigated directly, anticipating to the life expectancy and physical condition of the patient.

Final conclusions

Oncologic emergencies are acute, potentially life threatening conditions that have developed directly, or indirectly, as a result of malignant disease or cancer treatment. The clinical outcome of patients with symptoms caused by malignant disease is often poor and short-term mortality is high. In an emergency situation, estimating the prognosis and outcome of therapies is difficult. Many patients undergo invasive treatment, regardless of their cancer stage. Unbeneficial invasive therapies and costs of hospital care for patients with limited survival could be reduced when the extent of treatment is based on the patient's performance and the life expectancy. The consequences of interventions for the patient's quality of life should be thoroughly considered before commencing any treatment.

When treating severely ill patients, physicians need to be able to waive certain therapies. Currently, most decisions regarding emergency treatment, including invasive therapies, are being made without multidisciplinary evaluation. This is due to the fact that there is usually no opportunity for non-scheduled multidisciplinary discussion. If means could be developed to provide for such multidisciplinary decision making, this could very much improve clinical estimation of individual prognosis and outcome. Furthermore, the expert opinions of colleagues can be a support when difficult decisions have to be made. Defining the intention of prior cancer treatment and the performance score is essential for prognostication in emergency situations. However, related information is often confined in the acute setting, and a clinical estimation of the pre-existent physical condition is hard when a patient is critically ill. Determination of serum LDH and albumin levels and additional measurements of the handgrip strength can serve as objective parameters for the clinical judgment of the patient prognosis and outcome of treatment. In this way, treatment can be

adjusted to the individual life expectancy and physical condition, and overtreatment can be prevented.

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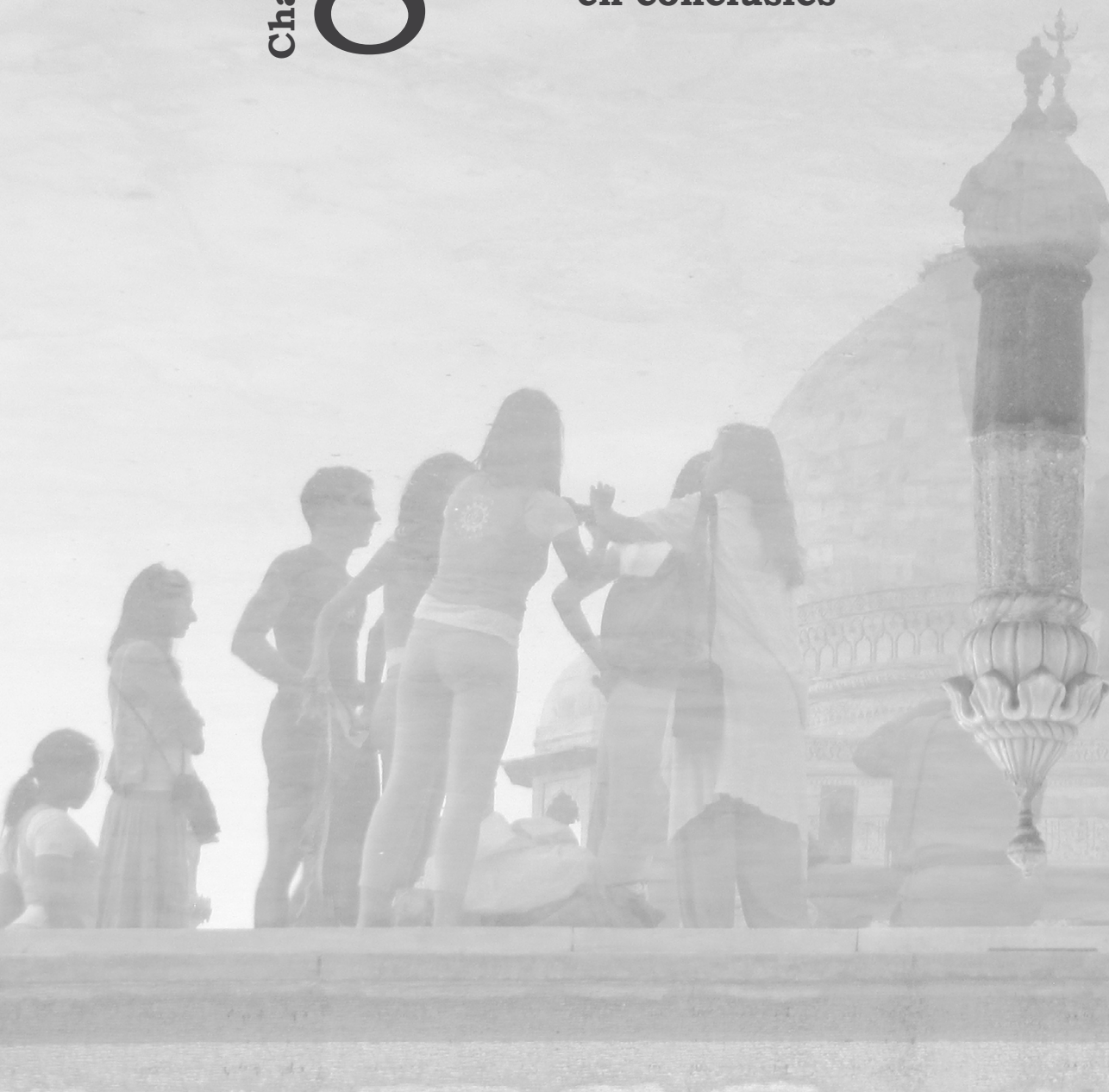
Chapter 8

Nederlandse samenvatting en conclusies



Spoedeisende chirurgisch oncologische problematiek Besluitvorming en klinische resultaten

Acute, potentieel levensbedreigende aandoeningen die, direct of indirect, zijn ontstaan ten gevolge van oncologische ziekte of behandeling worden beschouwd als spoedeisende oncologische problematiek [1,2]. Voor een groot deel van deze problemen is niet-electieve therapie noodzakelijk en soms zijn chirurgische ingrepen geïndiceerd voor de behandeling of (tijdelijke) verlichting van de symptomen [3,4]. In dit proefschrift is de huidige zorg voor patiënten met spoedeisende chirurgisch oncologische problematiek beschreven en is er gekeken naar de klinische resultaten van behandeling van deze patiëntencategorie. Dit is gedaan om het bewustzijn te vergroten met betrekking tot het vóórkomen van spoedeisende chirurgisch oncologische problematiek, de intensiteit van zorg die hiervoor wordt verleend en de gevolgen voor patiënten die deze problemen ervaren. Tevens is onderzocht of er parameters konden worden geïdentificeerd, die kunnen helpen bij het tijdig herkennen van patiënten die in hun laatste levensfase zijn en waarbij er afgezien zou moeten worden van operatieve behandeling.

In *Hoofdstuk 1* is inleidend de motivatie tot dit proefschrift uiteengezet. Sommige spoedeisende chirurgisch oncologische problemen zijn uitingen van vergevorderde oncologische ziekte. Het behandeltraject dat in een niet-electieve situatie wordt gekozen is vaak afhankelijk van de besluiten van een enkele dienstdoende arts. Deze eerste besluiten kunnen grote gevolgen hebben voor het beloop van de aandoening en de uitkomst van behandeling. Het is belangrijk dat in de besluitvorming rondom de behandeling van het acute probleem de prognose en de kwaliteit van leven van de patiënt worden meegewogen. Iedere behandeling heeft namelijk consequenties. Behandelingen kunnen soms ernstiger gevolgen hebben dan de aandoening zelf. Patiënten moeten fysiek in staat zijn te herstellen van het probleem waarvoor ze hulp zoeken, maar ook van de behandeling. Daarom dient invasieve behandeling enkel uitgevoerd te worden wanneer er een gunstig klinisch resultaat te verwachten is [5]. Wanneer behandeling niet zinvol lijkt, moet men hier ook in een acute situatie van durven afzien. Een structurele multidisciplinaire benadering, bijvoorbeeld binnen een team met leden die gespecialiseerd zijn in spoedeisende oncologische problematiek,

zou de besluitvorming optimaliseren. Hierdoor kan de besluitvorming efficiënter verlopen en kan, indien nodig, palliatieve zorg op kortere termijn worden ingezet. Aan het einde van het hoofdstuk zijn de verschillende onderwerpen van dit proefschrift besproken, die kunnen dienen als argumenten voor de noodzaak tot verbetering van de zorg voor patiënten met spoedeisende chirurgische problematiek.

Definitie en vóórkomen van spoedeisende chirurgisch oncologische problematiek

Bij oncologische patiënten kan zich een verscheidenheid aan spoedeisende chirurgische problemen voordoen. Deze kunnen zowel benigne als maligne van aard zijn. In *Hoofdstuk 2* is een overzicht gegeven van spoedeisende chirurgische problematiek die voor kan komen bij oncologische patiënten. Tevens werd er een overzicht gegeven van verschillende therapeutische opties voor deze problemen. Een veel voorkomend spoedeisend probleem bij oncologische patiënten is gastrointestinale obstructie. Obstructie kan naast de tractus digestivus ook optreden in andere organen of structuren. Dit kunnen bijvoorbeeld de urinewegen zijn, de luchtwegen, of het centrale zenuwstelsel. Overige spoedeisende chirurgisch oncologische problemen zijn gastrointestinale perforatie, bloedingen, infectieuze complicaties van oncologische behandeling en pathologische fracturen. Informatie met betrekking tot de performance status van de patiënt, het oncologische ziektestadium en de oncologische prognose is essentieel tijdens de besluitvorming rondom behandeling voor het optimale beleid. De complicaties van het oncologische probleem kunnen voor sommige patiënten ernstiger zijn dan de risico's van een interventie, terwijl voor anderen de interventie zelf een groter risico met zich meebrengt voor een nadelige uitkomst, of zelfs voor een kortere overleving. Welke behandeling dient te worden ingezet, chirurgisch of conservatief, zal voor iedere patiënt anders zijn.

Het is belangrijk dat de bewustwording wordt bevorderd met betrekking tot het vóórkomen van spoedeisende chirurgisch oncologische problematiek in de klinische praktijk en de klinische gevolgen hiervan. Daarom is in *Hoofdstuk 3* middels een retrospectieve analyse geëvalueerd wat redenen waren voor oncologische patiënten om de spoedeisende

hulp (SEH) te bezoeken voor chirurgische consultatie. Tevens is de mortaliteit van de patiënten na dit bezoek aan de SEH onderzocht. Van alle oncologische patiënten die zich gedurende een periode van zes maanden presenteerden op de SEH voor een chirurgisch consult, ervoeren 53,5% van de patiënten complicaties van oncologische behandeling. Verder presenteerden 25,5% van de patiënten zich met symptomen die veroorzaakt werden door oncologische ziekte en slechts 21% ervoer klachten die niet gerelateerd konden worden aan oncologische ziekte of behandeling. Intestinale obstructie was de meest voorkomende reden voor patiënten om zich te presenteren op de SEH en meer dan een derde van deze obstructieklachten (41,5%) bleek een maligne oorzaak te hebben. De mortaliteit na een bezoek aan de SEH was het hoogst voor de patiënten die zich presenteerden met symptomen veroorzaakt door oncologische ziekte. Gedurende de follow-upperiode was 62,8% van de patiënten uit deze categorie overleden en de mediane overlevingsduur was 69 dagen. Meer dan een derde van de overleden patiënten uit deze categorie was binnen 30 dagen na het SEH-bezoek overleden. Gezien deze hoge mortaliteit en korte overlevingsduur na een SEH-bezoek vanwege symptomen veroorzaakt door oncologische ziekte, is de overweging welke (intentie van) behandeling zinvol zal zijn voor oncologische patiënten op de SEH essentieel. De mortaliteit na SEH-bezoek was hoger voor patiënten waar werd afgezien van een chirurgische behandeling, dit in vergelijking met de patiënten die wel acute of electieve ingrepen ondergingen. De meeste patiënten die binnen de eerste 30 dagen waren overleden (89,5%) had geen chirurgische behandeling ondergaan. Dit zou mogelijk komen doordat er toch in een acute situatie een correcte inschatting van de fysieke toestand van de patiënt wordt gedaan, waardoor er wordt afgezien van behandeling wanneer er geen gunstig resultaat wordt verwacht.

Het huidige beleid en het klinische resultaat voor patiënten met spoedeisende chirurgisch oncologische problematiek

In een acute situatie is het niet eenvoudig een inschatting maken van de prognose en uitkomst van verschillende behandelopties. Een bezoek aan de SEH vanwege spoedeisende chirurgisch oncologische problematiek kan een teken zijn van vergevorderde ziekte met

een kans op overlijden op korte termijn. Naast de fysieke conditie van de patiënt en de levensverwachting, zouden het te verwachten effect en ook de kosten van behandeling moeten worden meegenomen in de beleidsbepaling. In *Hoofdstuk 4* is een overzicht gegeven van de ziekenhuiskosten voor oncologische patiënten na een bezoek aan de SEH voor chirurgische consultatie, in relatie met de overleving na dit SEH-bezoek. Voor patiënten die de SEH bezochten vanwege symptomen veroorzaakt door oncologische ziekte en die binnen 30 dagen na het SEH-bezoek overleden, waren deze ziekenhuiskosten beperkt, slechts €4.877. Deze kosten werden hoger worden naarmate de overleving langer duurde, maar waren in absolute termen nog steeds gering was (€27.999 voor patiënten overleden tussen 6 maanden en 1 jaar en €47.217 voor patiënten overleden tussen 1 jaar en 1,5 jaar). In ogenschouw nemend dat een Quality Adjusted Life Year (QALY) in Nederland € 50.000 mag kosten, zou men zich kunnen afvragen wat aanvaardbare kosten zijn voor behandelingen voor (oncologische) patiënten met een beperkte levensverwachting [6]. Een andere bevinding was dat een overzicht van ziekenhuiskosten op basis van DBC's is niet representatief lijkt voor de intramurale kosten en intensiteit van de zorg voor oncologische patiënten na een SEH-bezoek vanwege spoedeisende chirurgische problematiek. Er werden grote verschillen gezien tussen de geanalyseerde bedragen op basis van de geregistreerde DBC's en de bedragen op basis van de geregistreerde verrichtingen in het ziekenhuis (de absolute kosten). Deze absolute kosten waren in vergelijking hoger. Blijkbaar was de zorg die verleend werd intensiever dan op basis van de huidige DBC's wordt verwacht. De verschillen in bedragen waren voornamelijk groot voor de patiënten die zich presenteerden met symptomen veroorzaakt door oncologische ziekte; de patiëntencategorie met de slechtste prognose en de hoogste mortaliteit. Een overlijden is niet altijd te verwachten naar aanleiding van een SEH-bezoek, maar indien patiënten reeds tekenen van progressieve oncologische ziekte hebben is de prognose vaak somber. Door te anticiperen op de levensverwachting kunnen overbehandeling en kosten worden beperkt, zonder daarbij afbreuk te doen aan de kwaliteit van leven. Wanneer overlijden op korte termijn te verwachten is, zou een optimale kwaliteit van leven de hoogste prioriteit moeten hebben. Maximale zorg betekent niet altijd optimale zorg. Hoge zorgkosten rondom het levenseinde gaan niet gepaard met een betere overleving en leiden ook niet tot een betere kwaliteit van overlijden [7-9].

Oncologische patiënten ontvangen vaak behandelingen van verschillende medische disciplines. De optimale manier van medische besluitvorming bij complexe (oncologische) problematiek is middels een gezamenlijke benadering. In de meeste oncologische richtlijnen

wordt daarom ook geadviseerd om de diagnostiek, behandeling en follow up te doen plaatsvinden binnen een multidisciplinair team. Echter, in acute situaties is overleg in een multidisciplinaire setting meestal niet mogelijk. Beslissingen met betrekking tot het wel of niet uitvoeren van acute invasieve behandeling worden vaak door een enkele arts gemaakt. In *Hoofdstuk 5* is geanalyseerd of patiënten met spoedeisende chirurgisch oncologische problematiek werden besproken in een multidisciplinair overleg, of zij chirurgische behandeling ondergingen en wat de klinische gevolgen voor deze patiënten waren na een periode van 30 dagen. Tijdens de follow-up periode onderging 40% van de patiënten een chirurgische behandeling na een mediane periode van 38 uur na presentatie. Het grootste deel van deze ingrepen (84%) was niet electief. Dit hoofdstuk liet zien dat niet-electieve invasieve behandeling, zoals chirurgie, in de meeste gevallen werd uitgevoerd zonder dat de patiënt werd besproken in een multidisciplinair overleg. Slechts 30% van alle patiënten werd multidisciplinair besproken na een mediane periode van 12 dagen na presentatie. Dit in weerwil van het feit dat meerdere medische specialismen betrokken waren bij het behandelproces. Van de patiënten die een chirurgische behandeling ondergingen werd 41% multidisciplinair besproken, echter bij het grootste deel (79%) van deze patiënten vond dit overleg pas plaats na de chirurgische behandeling. Het proces bij deze patiënten met spoedeisende chirurgisch oncologische problematiek kwam dus niet overeen met de algemene oncologische richtlijnen [10-13]. Een groot deel van de patiënten die spoedeisende chirurgisch oncologische problemen ervoeren waren voor inclusie al gediagnosticeerd met gemetastaseerde ziekte, of bleken gedurende de korte follow-up periode van 30 dagen gemetastaseerde ziekte te hebben. De 30-dagen mortaliteit voor alle patiënten met spoedeisende chirurgisch oncologische problematiek was 12,6%. Een aanzienlijk deel (46%) van de patiënten kwam in een palliatief stadium en/of overleed op zeer korte termijn. Het hoofdstuk benadrukte het ontwikkelen van acute oncologische zorgpaden die ook in spoedeisende situaties voorzien in structurele multidisciplinaire benadering, waar bij voorkeur de behandelende huisarts wordt betrokken [14]. Dit zal resulteren in het sneller inzetten van de meest geschikte individuele behandeling en het vermijden van overbodige onderzoeken of zinloze invasieve therapie aan het levenseinde.

Risico inschatting

Het ontstaan van spoedeisende chirurgisch oncologische problematiek kan een teken zijn van vergevorderde ziekte en het klinische resultaat is vaak ongunstig. Wanneer men in staat zou zijn om patiënten die in de laatste levensfase zijn tijdig te herkennen, kunnen overbodige en belastende onderzoeken of behandeling vermeden worden met behoud van de kwaliteit van leven [8,15-17]. In acute situaties moet men soms snel handelen. Vaak is recente informatie met betrekking tot het oncologische ziektestadium en de functionele status voorafgaand aan de spoedopname onvolledig of niet beschikbaar. Er is behoefte aan parameters die eenvoudig en snel bepaald kunnen worden, die kunnen dienen als hulpmiddel voor het schatten van de prognose en conditie van de patiënt en dus ook voor het krijgen van inzicht in de uitkomst van het spoedeisende probleem en eventuele behandeling. In *Hoofdstuk 6* zijn verschillende patiëntenkarakteristieken en parameters geëvalueerd om te kijken of zij geassocieerd waren met overlijden op korte termijn na een spoedeisend chirurgisch oncologisch probleem. Het definiëren van de intentie van voorafgaande oncologische behandeling en de performance score bleken nuttige informatie te zijn voor het inzicht in het klinische resultaat. Deze gegevens kunnen dienen als argumentatie bij besluitvorming met betrekking tot de intensiteit van acute behandeling. In een acute situatie is bij een ernstig zieke patiënt de performance van een patiënt echter lastig in te schatten. Tevens is informatie over de voorgeschiedenis van de patiënt vaak beperkt. Bij gebrek aan handvatten en argumentatie om af te zien van therapie wordt er daarom toch invasief gehandeld. In dit hoofdstuk werden aanvullende parameters onderzocht op hun prognostische waarde na het doormaken van spoedeisende chirurgisch oncologische problemen. Een hoog LDH en een laag albumine in het serum, tevens lage knijpkracht bleken geassocieerd met overlijden op korte termijn. Deze parameters kunnen derhalve helpen bij een (objectieve) klinische inschatting van de individuele prognose in acute situaties. Zo kan er vanaf het begin behandeling worden ingesteld die afgestemd is op de levensverwachting en de fysieke toestand van de patiënt.

Eindconclusies

Acute, potentieel levensbedreigende aandoeningen die, direct of indirect, zijn ontstaan ten gevolge van oncologische ziekte of behandeling, worden beschouwd als spoedeisende oncologische problematiek. De klinische uitkomst van patiënten met symptomen veroorzaakt door oncologische ziekte is vaak ongunstig en de mortaliteit op korte termijn is hoog. In een acute situatie zijn het schatten van de prognose en voorspellen van de resultaten van behandeling niet eenvoudig. Veel patiënten ondergaan invasieve behandeling, ongeacht het oncologische ziektestadium. Onnodige invasieve ingrepen en ziekenhuiskosten voor patiënten met geringe overleving kunnen beperkt worden wanneer de intensiteit van behandeling wordt afgestemd op de performance van de patiënt en de levensverwachting. De invloed van een interventie op de kwaliteit van leven van de patiënt moet zorgvuldig worden overwogen voordat enige vorm van behandeling wordt ingezet.

Ook wanneer een patiënt ernstig ziek is moeten artsen in een acute situatie durven afzien van behandeling. De meeste beslissingen rondom acute behandeling, inclusief invasieve ingrepen, worden genomen zonder multidisciplinaire evaluatie. Dit komt doordat deze buiten de reguliere geplande momenten niet beschikbaar is. Multidisciplinaire evaluatie zou de klinische inschatting van de individuele prognose en uitkomst kunnen verbeteren. Daarnaast bieden standpunten van collega experts steun wanneer lastige besluiten moeten worden genomen. Het definiëren van de intentie van voorgaande oncologische behandeling en van de performance van de patiënt is essentieel voor prognosestelling in een acute situatie. Echter, gedocumenteerde informatie hierover is in de acute setting vaak beperkt en een klinische inschatting van de pre-existente fysieke conditie is niet eenvoudig wanneer een patiënt ernstig ziek is. Bepalingen van het serum LDH en albumine en aanvullende metingen van de knijpkracht kunnen dienen als objectieve parameters voor de klinische beoordeling van de individuele prognose en het klinische resultaat van behandeling. Zo kan therapie worden afgestemd op de individuele levensverwachting en fysieke conditie en kan overbehandeling worden voorkomen.

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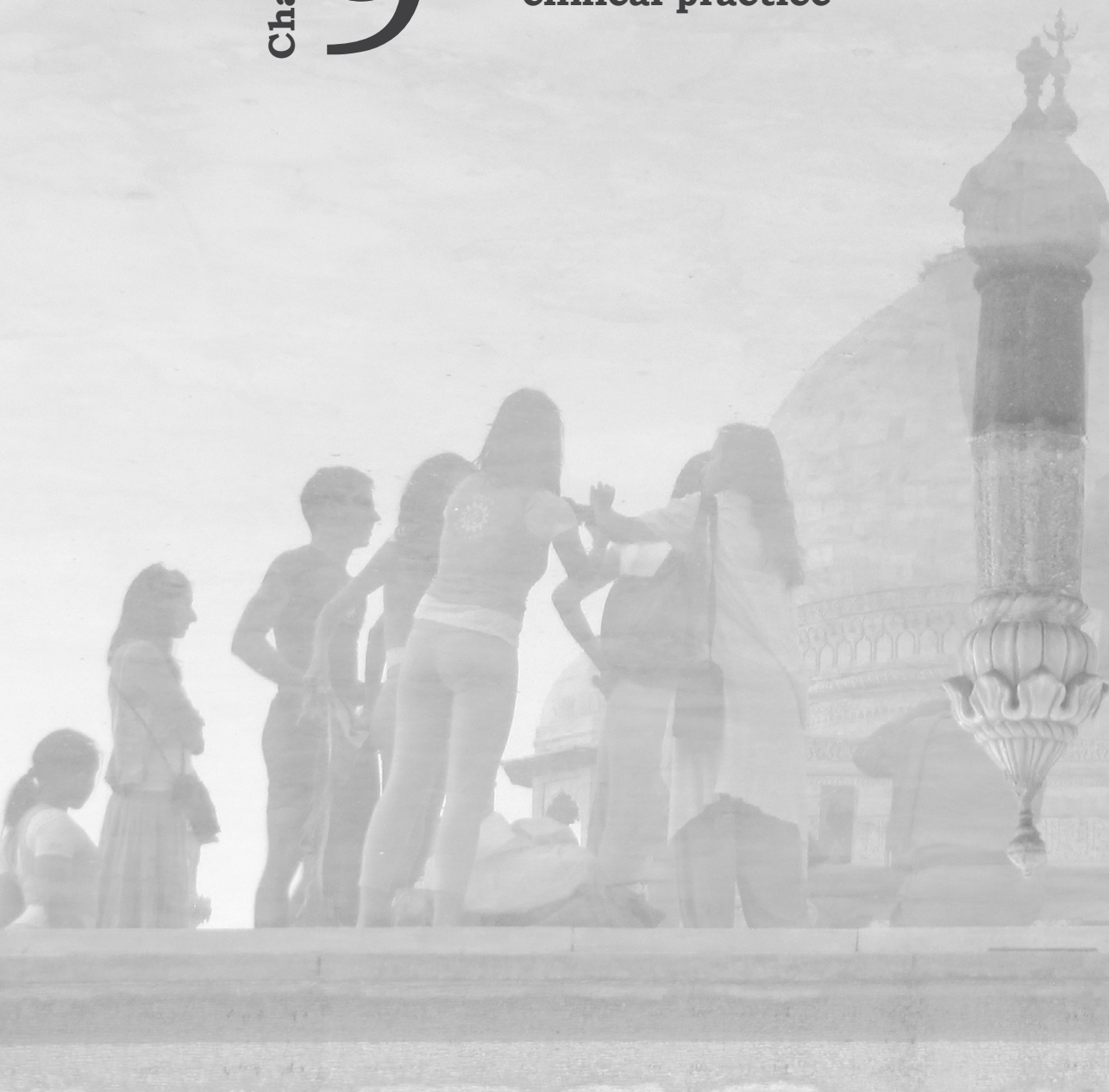
Chapter 9

Recommendations for clinical practice



As described in this thesis, the outcome of patients after surgical oncologic emergencies is often poor. Patients with oncologic emergencies are often initially examined and cared for by physicians from emergency services. Due to shortage of staff outside of office hours, management of the emergency often depends on the personal decisions of a single physician who, in many cases, will be unfamiliar with (the medical history of) the individual patient. As this is undesirable, conditions should be created for better informed medical treatment. Also in an emergency situation, cancer patients should receive treatment that not only suits the patient's wishes, but also takes into account the individual prognosis, part of which is the patient's ability to recover from the intervention. In this way, the patient's care and quality of life will be secured as reliably as possible.

The first step in the modification of current emergency care for cancer patients should be raising the general awareness of the nature of (surgical) oncologic emergencies, together with the knowledge regarding the consequences that they may have. If this is achieved, early signaling of oncologic emergencies can be secured and primary management can be improved. For this thesis, one of the first extensive registrations of surgical oncologic emergencies has been performed and the subsequent clinical outcome was explored. Hopefully, the results that have been presented will contribute to the general awareness of physicians and change their clinical management.

A second step that would improve clinical practice would be further development and validation of parameters and tools for prediction of outcome in the oncologic emergency setting. If and when these tools are available and implemented in general care, physicians will be able to discuss possible outcomes of treatment with their patients, and perhaps more importantly, recognize cancer patients who are at the end of life. Early and reliable assessment of the patient's performance is essential in the treatment process. Patients need to be able to recover from emergency interventions, which in turn need to improve the emergency situation. Therefore, the intent and extent of emergency care should not only be derived from the prognosis of the emergency situation, but also from the individual performance and cancer prognosis in more general terms. Overtreatment should be avoided, especially at the end of life.

While there is a trend to educate emergency physicians in palliative care, the emergency department is generally considered to be a temporary residence for diagnosing and/or resuscitation, and often not the place for the determination of definitive treatment. The decision to withhold treatment from patients is difficult, and physicians who are not educated in (emergency) cancer care may see hospital admission as a way to avoid making this decision. For patients who face the end of life, hospital admission may result in unnecessary diagnostics and treatment, and thereby cause delay in the institution of palliative end-of-life care, which is often delivered in home situations. On the other hand, when patients could benefit from invasive therapies, there should be no delay in providing emergency treatment.

Ideally, a third step would ensure that all cancer patients who experience oncologic emergencies would always be evaluated by a team of physicians who have experience treating these emergencies. Decisions regarding treatment in emergency situations are often difficult, and a multidisciplinary team would consider alternatives and agree upon the best course of action. Multidisciplinary cancer conferences are generally designed for electively treated patients and take place following a preordained schedule. Specialized oncology teams for multidisciplinary decision making, are usually not available in emergency situations, and obviously, having to wait for the next multidisciplinary meeting will delay the institution of final treatment. In cases when treatment is required immediately, interventions are often performed on the basis of individual decisions. For patients who require non-elective treatment, non-scheduled multidisciplinary evaluation by acute oncology experts should be available.

The introduction of acute oncology pathways, based on structural availability of a dedicated multidisciplinary team, will enhance the efficiency of emergency cancer care and reduce the duration of hospital stay and costs. If established, the members of these teams must be specialized in care for patients with oncologic emergencies and should be available for non-elective consultation in the emergency room and hospital wards. An acute oncology care team would ideally include (at least) an emergency care specialist, a medical oncologist, a surgical oncologist, a radiation oncologist, an oncology nurse, and a palliative care specialist. These teams could enhance their effectiveness by developing close contacts with general practitioners, nursing homes, and hospices. Depending on the health care and hospital financial systems, the make-up of these teams and the way they operate should

be organized on the same basis as other dedicated teams and specialized services within general hospital care.

These acute oncology specialists should be involved in the treatment process immediately after the first emergency contact with a cancer patient. The primary physician should be part of the multidisciplinary team, and the responsibility of care for these patients will lie with this specialized team. All treatment decisions will be made in a multidisciplinary setting. In this way, the type of treatment will not depend on the personal decisions of only one professional. If patients are not expected to benefit from invasive treatment, they could be referred to supportive end-of-life care at the earliest opportunity, thanks to earlier recognition and improved coordination.

Acute oncology teams are a new phenomenon and should be implemented in standard hospital care. These teams will represent a new medical discipline; i.e. acute oncology care. While such teams resemble palliative care teams, they are different in the sense that if necessary, invasive (non-) palliative, or curative care can be provided as well. Oncology care could improve substantially if all cancer patients who require emergency treatment receive appropriate, individualized treatment without any unnecessary delay. The outcome and quality of life should have the highest priority when treatment decisions are made.

Appendices

List of publications

List of publications

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Dankwoord

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Curriculum vitae

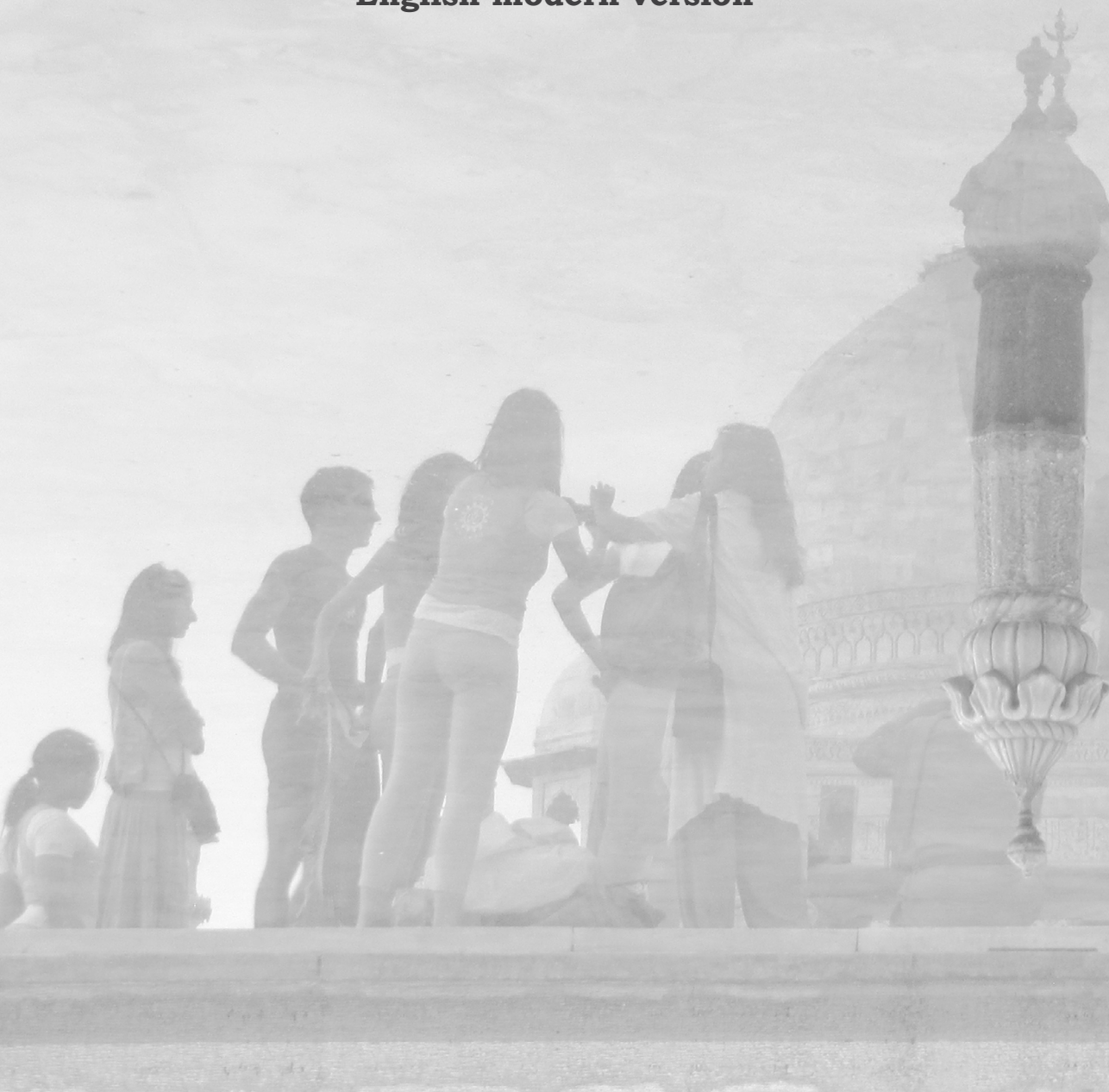
Frederiek Bosscher werd geboren op 1 april 1986 in Groningen. Zij is de jongste dochter van Doeko Bosscher en Roberta Sellies en het zusje van Robert, Annette en Lisa. Ze groeide op in de stad Groningen en na het behalen van haar VWO-diploma aan het Praedinius Gymnasium studeerde ze geneeskunde aan de Universiteit van Amsterdam (UvA).

Tijdens haar studententijd was ze actief in meerdere commissies en besturen. Ze organiseerde onder andere buitenlandse stages voor geneeskunde studenten en was actief betrokken bij de ontwikkeling van de Master geneeskunde aan de UvA. In het vierde jaar van haar studie deed ze gedurende 5 maanden een wetenschappelijke stage in het Computer Assisted Surgery Center van the Hospital for Special Surgery in New York City, een orthopedisch ziekenhuis. Hier werkte ze mee aan een onderzoeksproject naar factoren van invloed op de stabiliteit van knieën met voorste kruisband deficiëntie. Haar studie sloot zij af met een keuzecoschap chirurgie in Tanzania en een oudste coschap op de afdeling abdominale chirurgie in het Academisch Medisch Centrum (AMC).

Na het behalen van het artsexamen in juli 2012 keerde ze terug naar het hoge noorden en werkte een jaar als ANIOS chirurgie in het Universitair Medisch Centrum Groningen (UMCG). Onder leiding van prof. dr. H.J. Hoekstra en dr. B.L. van Leeuwen zette zij vervolgens een onderzoeksproject op rondom spoedeisende chirurgische problematiek bij oncologische patiënten. Gedurende een jaar werkte zij als arts-onderzoeker en de onderzoeksresultaten uit deze periode hebben geleid tot dit proefschrift.

In januari 2015 is ze begonnen met de opleiding Heelkunde in regio VI, waarvan de eerste jaren zullen plaatsvinden in het Universitair Medisch Centrum Groningen en het Medisch Spectrum Twente, onder begeleiding van de opleiders prof. dr. E. Heineman en dr. J.M. Klaase.

Hippocratic Oath
English modern version



Hippocratic oath

English modern version

Written in 1964 by Louis Lasagna, Academic Dean of the School of Medicine at Tufts University, and used in many medical schools today.

I swear to fulfill, to the best of my ability and judgment, this covenant:

I will respect the hard-won scientific gains of those physicians in whose steps I walk, and gladly share such knowledge as is mine with those who are to follow.

I will apply, for the benefit of the sick, all measures [that] are required, avoiding those twin traps of overtreatment and therapeutic nihilism.

I will remember that there is art to medicine as well as science, and that warmth, sympathy, and understanding may outweigh the surgeon's knife or the chemist's drug.

I will not be ashamed to say "I know not," nor will I fail to call in my colleagues when the skills of another are needed for a patient's recovery.

I will respect the privacy of my patients, for their problems are not disclosed to me that the world may know. Most especially must I tread with care in matters of life and death. If it is given me to save a life, all thanks. But it may also be within my power to take a life; this awesome responsibility must be faced with great humbleness and awareness of my own frailty. Above all, I must not play at God.

I will remember that I do not treat a fever chart, a cancerous growth, but a sick human being, whose illness may affect the person's family and economic stability. My responsibility includes these related problems, if I am to care adequately for the sick.

I will prevent disease whenever I can, for prevention is preferable to cure.

I will remember that I remain a member of society, with special obligations to all my fellow human beings, those sound of mind and body as well as the infirm.

If I do not violate this oath, may I enjoy life and art, respected while I live and remembered with affection thereafter. May I always act so as to preserve the finest traditions of my calling and may I long experience the joy of healing those who seek my help.