research article

Analysis of emergency head computed tomography in critically ill oncological patients

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Background. Critically ill cancer patients have an increased risk of developing acute neurological signs. The study objective was to evaluate the use and the usefulness of emergency head computed tomography (EHCT) in this category of patients.

Patients and methods. This retrospective, single-centre, cohort study included patients with EHCT performed during Intensive Care Unit (ICU) admission for a period of three years. Indications, imagistic findings, type of malignancy, and outcome were evaluated to identify diagnostic yield and correlations between abnormal findings on positive scans, malignancy type, and mortality rate.

Results. Sixty-four EHCTs were performed in 54 critically ill cancer patients, with 32 scans (50%) showing previously unknown lesions and considered to be positive. The most frequent abnormal findings were ischemic (15 EHCTs, 47%) and haemorrhagic (13 EHCTs, 40%) lesions. Thirty-eight EHCTs (59%) were indicated for altered mental status, with a positivity rate of 50%. Eighteen EHCTs (48%) were performed in hematological malignancy patients: 9 (50%) of which were positive with 8/9 (89%) displaying hemorrhagic lesions. Twenty EHCTs were performed in solid tumour patients, 10 (50%) of which were positive, with 9/10 (90%) displaying ischemic lesions. Out of 54 patients, 30 (55%) died during ICU stay. The mortality rate was higher in patients with hematological malignancies and positive EHCT (78% *vs*. 58%).

Conclusions. Diagnostic yield of EHCT in critically ill cancer patients is much higher than in other categories of ICU patients. We support the systematic use of EHCT in critically ill, mainly hemato-oncological patients with nonspecific neurological dysfunction, as it may lead to early identification of intracranial complications.

Key words: emergency head CT; altered mental status; cancer; critically ill; neurological complications

Introduction

Acute neurological dysfunction is common in patients admitted to the Intensive Care Unit (ICU) with a wide spectrum of neurological findings including depressed consciousness, delirium, seizures and focal neurological signs.[1] Underlying etiologies include, but are not limited to, stroke (due to hemodynamic instability and coagulation abnormalities), use of sedative drugs, systemic inflammatory response and metabolic and endocrine disturbances.[2]

Emergency head computed tomography (EHCT) is often performed in critically ill patients to investigate neurologic signs and symptoms, such as focal neurologic deficits and seizure activity. The utility of imaging for patients who develop nonspecific altered mental status (AMS) is unclear.[3] AMS is a broad term, and can imply either change in consciousness (supratentorial function) or in

arousal (executed by the brainstem). Underlying etiologies include both systemic and central nervous system processes, the latter encompassing both organic and functional causes. The complex differential diagnosis can make AMS a potentially vexing clinical problem.[4]

Obviously, EHCT can provide important information for patient management, but in critically ill patients there are risks associated with transport and examination.[3] In addition, the financial expenses of possible unnecessary testing should also be taken into consideration.[5] Therefore, an EHCT request in an ICU patient should be carefully assessed, in order to decide if the potential benefits outweigh the risks.

Studies on head CTs use and appropriateness in critically ill medical and surgical patients were previously conducted, to assess the usefulness of clinical variables in selecting patients to be scanned[2,6,7] or to provide estimates of the frequency of acute changes on head CTs and therefore, their diagnostic yield.[3,8-10]

Critically ill oncological patients have an increased risk of developing acute neurological dysfunction due to several reasons. Sepsis is the most frequent cause of ICU admission in oncological patients; therefore, septic encephalopathy is common. Multiple organ dysfunction increases the risk for metabolic neurological dysfunction related to renal, hepatic or electrolytic disturbances. Thrombocytopenia and coagulation abnormalities predispose to intracranial bleeding. Central nervous system metastasis/infiltration by malignant cells may be present. The differential diagnosis of putative processes is challenging in these complex circumstances.

Therefore, the primary aim of this study was to evaluate EHCT diagnostic yield in a cohort of oncological patients treated in a mixed, non-neurosurgical ICU. Furthermore, we evaluated the distribution of positive EHCT according to the type of malignancy (hematological or solid tumour) and the relationship between positive EHCT and clinical indications. Finally, we evaluated the patients' outcomes related to their EHCT results.

Patients and methods

Study design

The study was performed in the Regional Institute of Oncology, Iasi, Romania, a 300-bed teaching hospital providing all types of antineoplastic treatment (surgery, chemo-, radio-, hormone- and immunotherapy). Neurosurgery is not performed in our institution; thus, the cohort of oncological patients did not include neurosurgical patients, who have specific indications for EHCT.

This retrospective, single-centre, cohort study included all patients admitted to our 11-beds ICU for a period of 3 years, with at least one EHCT performed during ICU admission, as indicated by the intensivist/neurologist. The medical charts of the included patients were reviewed. The scanned patients were identified using the Radiology and Imaging Department records. Data were extracted from electronic medical records, CT reports, CT scan request forms and ICU charts. We extracted demographic information, comorbidities, risk factors for stroke, hospital/ICU admission/discharge data, ICU admission diagnosis, type of malignancy (hematological or solid tumour), clinical indication for EHCT, contrast or non-contrast agent EHCT, platelet count and coagulation profile, and outcome.

Indications for EHCT

We assessed the indications for EHCT using the CT request forms and relevant physician notes in the ICU charts. Head CT exclusion criteria included indications related to craniofacial cancers (diagnostic or follow-up CT); head trauma during hospitalisation (e.g., falling from the same level during a syncopal state); missing information about the clinical indication; and missing CT report. One head CT was also excluded due to a massive lung bleeding, so the scan could not be completed.

Indications of EHCT were recorded as: (1) AMS, (2) focal neurologic deficit (FND), (3) seizure activity, or (4) other. AMS was defined as an alteration in consciousness or cognition documented in the charts as assessed by clinical examination. FND was identified by screening patients' medical charts for key phrases within the documentation of neurologic examinations performed by ICU physicians or neurology consultants. These key phrases indicative for neurologic abnormalities: new cranial nerve deficit, motor or sensory unilateral limb deficit or reflex abnormalities. Seizure activity was also identified during the review of charts. Other CT scan indications included persistent headache, re-evaluation after a previous scan, or post-anoxic encephalopathy. For patients who had more than one indication for EHCT, all were recorded in our database. Also, multiple scans for the same patient during the ICU stay were introduced in the database alongside the recorded clinical indications.

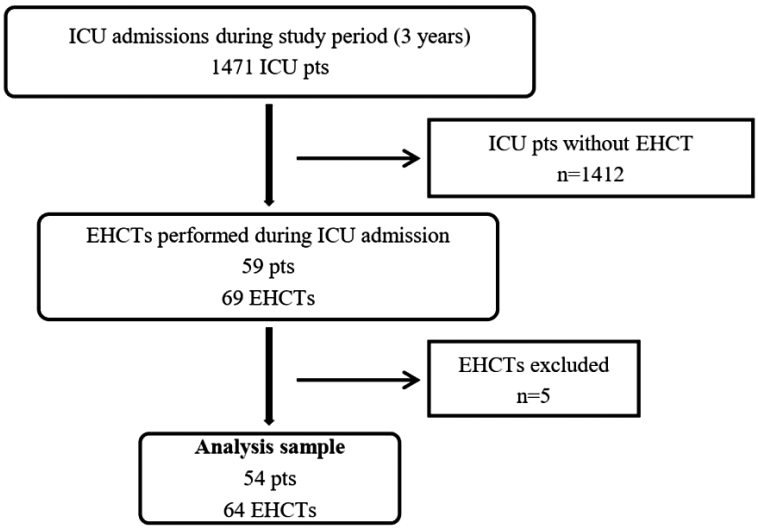

FIGURE 1. Study flowchart.

Interpretation of head CTs

All the EHCTs were interpreted by radiologists from the Radiology and Imaging Department. The CT reports were retrospectively scored as positive or negative by the study team. A positive EHCT was defined as one that found any previously unknown intracranial abnormality that could correlate with the clinical indication. All hemorrhagic lesions (intracerebral, subarachnoid, and intraventricular hemorrhage) were counted as „intracranial hemorrhagic lesions". Also, concomitant lesions on the same CT scan were counted, so abnormal findings consequently outnumbered positive EHCTs.

Statistical analysis

Data were analyzed using MedCalc Statistical Software version 19.1.7 (MedCalc Software Ltd, Ostend, Belgium; https://www.medcalc.org; 2020). Variables distribution assumptions were tested for normality using histograms and the Shapiro-Wilk test. Comparisons between normally distributed continuous variables were performed using Student's t-test. Comparisons between non-normally distributed continuous variables were performed using the Mann-Whitney U-test. Comparisons between categorical variables were performed using the Chi-squared test or Fisher's exact test.

Categorical variables were presented as number (n) and percentage (%). Continuous variables were presented as mean and standard deviation (SD) if normally distributed, or as median and interquartile range (IQR) if non-normally distributed.

Ethical issues

The study was approved by the Research Ethics Committee of the Regional Institute of Oncology Iasi. Being a retrospective study, an informed consent waiver was issued.

Results

Study group

A total of 1471 patients from three hospital departments, namely: Oncological Surgery, Oncology, and Hematology, were admitted to ICU during the study period. These patients were mostly men (55%), with a mean age of 63.0 ± 12.5 years, and 522/1471 (35.5%) had hematological malignancies. The median ICU length of stay (LOS) was 6.5 (3–9) days, 400 patients (27.2%) died during their ICU hospitalization.

In the study period 69 head CT scans were performed for 59 ICU patients, representing 4% of ICU-admitted patients. Five head CTs performed for five patients were excluded for reasons mentioned above. At the end, the analysis sample included 64 EHCTs for 54 ICU patients (Figure 1). Intravenous contrast agent was used in 39 (57%) EHCTs in 34 (63%) patients, according to clinical indications and patient comorbidities (e.g., renal failure).

The EHCT patients had similar characteristics in terms of gender, age, and malignancy type distribution to the whole group of ICU-admitted patients. The median ICU LOS of EHCT patients was higher than the general median ICU LOS (10.5 *vs*. 6.5 days). The ICU mortality of EHCT patients was twice the general ICU mortality (55% *vs*. 27.2%), (Table 1).

Indications for EHCT

Out of 64 EHCTs, 18 (28%) had more than one clinical indication. Thirty-eight scans (59%) were indicated for AMS, 21 (32%) for FND and 7 (11%) for seizure. As expected, the proportion of positive EHCTs indicated for FND (13/21, 62%) and for seizure (5/7, 71%) was higher than the proportion of positive EHCTs indicated for AMS (19/38, 50%). The number of positive EHCTs indicated for other reasons was significantly lower (3/16, 18%), (Table 2).

Positive EHCT

In the group with positive EHCT, 24 (44%) out of 54 patients had previously unknown lesions (Table 1). When analyzing positive EHCTs, 32 (50%) scans out of 64, showed previously unknown lesions (Table 2).

Abnormal findings on positive EHCT

When analyzing the positive EHCTs, the abnormal findings were: ischemic lesions, intracranial hemorrhagic lesions, cerebral oedema, brain metastases, leukemic infiltration, arteriovenous brain malformation, solid tumours, and hydrocephalus (Table 2). Abnormal findings with the highest frequencies were ischemic and hemorrhagic lesions. Their distributions were further analyzed according to EHCT indications (Table 3).

Because AMS was the most frequent nonspecific indication for scanning, we analyzed abnormal findings on EHCT performed for this indication. Out of 38 scans indicated for AMS, 18 (48%) were performed in hematological patients: 9 (50%) of which were positive, with 8/9 (89%) hemorrhagic and 2/9 (21%) ischemic lesions. In 18 patients with solid tumours, 20 EHCTs were performed for AMS, and 10 (50%) of which were positive 9/10 (90%) were ischemic and 2/10 (20%) displayed hemorrhagic lesions.

Outcome

Out of 54 patients, 30 (55%) died during ICU hospitalization. The mortality was similar in patients with positive (58%) *vs.* negative (53%) EHCT, but higher in patients with hematological malignancies and positive EHCT *vs.* negative EHCT (7/9, 78% respectively 7/12, 58%), (Table 4).

Twenty-two out of 30 patients (73%) with EHCT indicated for AMS died in the ICU. The mortality of haematological patients with AMS was higher for positive (6/7, 85%) than negative (6/9, 67%) EHCTs, (Table 5).

Discussions

Our study showed a high rate of newly diagnosed intracranial processes by EHCT in a cohort of non-neurosurgical oncological patients admitted to ICU for non-neurological reasons. Exclusion of neurosurgical patients is worth mentioning, because this class of patients demands more scans for diagnosis and follow-up, usually with a higher probability of positive findings.

The main indications for EHCTs in our study were FND/seizure. Analyzing the newly diagnosed

TABLE 1. Characteristics of EHCT patients

Variables	Overall (*n* = 54)	(+) EHCT (*n* = 24)	(-) EHCT (*n* = 30)	*p* value
Age	61 (12.7)	62 (13.2)	60 (12.4)	0.74
Gender				
Male	28 (51.9)	16 (67.7)	12 (40.0)	0.05
Female	26 (48.1)	8 (33.3)	18 (60.0)	
Malignancy type				
Solid tumour	33 (61.1)	15 (62.5)	18 (60.0)	0.85
Haematological malignancy	21 (38.9)	9 (37.5)	12 (40.0)	
Outcome				
ICU LOS	10.5 (6–14)	8.5 (4–11)	12.5 (7–15)	0.03
Hospital LOS	18 (12–30)	15.5 (10–26)	20.0 (14–34)	0.10
ICU mortality	30 (55.6)	14 (58.3)	16 (53.3)	0.71

Variables are presented as number (%), mean (standard deviation [SD]) or median (interquartile range [IQR]).

EHCT = emergency head computed tomography; ICU = Intensive Care Unit; LOS = length of stay; *n* = number

TABLE 2. Characteristics of ECHTs

Variables	EHCT (*n* = 64)	(+) EHCT (*n* = 32)	(-) EHCT (*n* = 32)	*p* value
Indications				
Altered mental status	38 (59.4)	19 (59.4)	19 (59.4)	1.00
Focal neurological deficits	21 (32.8)	13 (40.6)	8 (25.0)	0.27
Seizures	7 (10.9)	5 (15.6)	2 (6.2)	0.26
Other	16 (25.0)	3 (9.4)	13 (40.6)	< 0.01
Results				
Ischemic stroke	15 (23.4)	15 (46.9)		
Haemorrhagic lesions	13 (20.3)	13 (40.6)		
Cerebral oedema	10 (15.6)	10 (31.2)		
Brain metastases	5 (7.8)	5 (15.6)		
CNS infiltrates	1 (1.6)	1 (3.1)		
Arterio-venous malformation	2 (3.1)	2 (6.2)		
Hydrocephalus	1 (1.6)	1 (3.1)		
Primary brain tumour	2 (3.1)	2 (6.2)		

Variables are presented as number (%).

EHCT = emergency head computed tomography; n = number

TABLE 3. Distribution of ischemic and haemorrhagic lesions according to EHCTs indications

Indications for EHCT	(+) EHCT (*n* = 32)	Ischemic stroke (*n* = 15)	Haemorrhagic lesions (*n* = 13)	*p* value
Altered mental status	19 (59.4)	11 (28.9)	10 (26.3)	0.80
Focal neurological deficits	13 (40.6)	5 (23.8)	6 (28.6)	0.73
Seizures	5 (15.6)	1 (14.3)	1 (14.3)	-
Other	3 (9.4)	1 (6.2)	0 (0.0)	-

Variables are presented as number (%).

EHCT = emergency head computed tomography; n = number

TABLE 4. Mortality in patients with positive and negative EHCTs

Patients	Total	Solid tumours	Haematological tumours
EHCT+, all	24	15	9
EHCT+, dead (%)	14 (58)	7 (46)	7 (78)
EHCT-, all	30	18	12
EHCT-, dead (%)	16 (53)	9 (50)	7 (58)

EHCT = emergency head computed tomography

TABLE 5. Mortality in patients with positive and negative EHCTs indicated for AMS

Patients with AMS	Total	Solid tumours	Haematological
AMS & EHCT+, all	13	6	7
AMS & EHCT+, dead (%)	10 (76)	4 (67)	6 (85)
AMS & EHCT-, all	17	8	9
AMS & EHCT-, dead (%)	12(70)	6 (75)	6 (67)

AMS = altered mental status; EHCT = emergency head computed tomography

intracranial processes, we found a higher rate of hemorrhagic lesions in hematological patients and ischemic lesions in solid tumour patients. All patients were undergoing antineoplastic treatment at the time of ICU admission, i.e.: chemotherapy for hematological patients and chemotherapy, radiotherapy, or surgery for patients with solid tumours. Along with other recognized risk factors specific for critical illness (e.g., septic encephalopathy, residual sedation, immobilization, comorbidities), antineoplastic treatment adds to risk factors for neurological complications. Hematologic malignancies and chemotherapy usually lead to thrombocytopenia and coagulation disorders, predisposing to intracranial bleeding. On the other hand, inflammation associated with antineoplastic treatments in solid tumours significantly increases ischemic risk in patients who already have a procoagulant status. These features explain the distribution pattern of abnormal radiologic findings among patients and seem to be related to their outcomes.

ICU physicians are often faced with the dilemma of selecting the most appropriate diagnostic test for their patients. CT is widely used in critically ill patients due to its availability, accessibility, no need for compatible devices, and shorter duration, and is indicated for many clinical reasons in a wide range of suspected pathology.[10] Cerebral magnetic resonance imaging (MRI) is a superior diagnostic tool for critically ill patients with neurological disturbances. Compared with CT, MRI has an increased diagnostic sensitivity for acute stroke, neoplasms, infections and encephalopathy due to hypoxia, sepsis, uremia, hyperammonemia, glucose and sodium abnormalities.[12] Comparing CT and MRI performed in critically ill patients during the same ICU admission, the MRI diagnostic yield was better by 33%, but changed the CT based working diagnosis for only 4.4% of patients.[11] In addition, MRI has numerous safety challenges in ICU patients, the particular one being the need for MRI-compatible monitoring and life-support equipment. Considering the risk-benefit ratio, MRI indications in critically ill patients should probably include request for additional assessment of CT findings and evaluation of patient with persistent neurologic symptoms despite a normal/equivocal CT.

The associated risks and costs of every investigation must be weighed against the failure of a correct diagnosis. Moreover, in oncological patients, it is difficult to keep a good balance between under- and over-imaging, mainly in the case of non-specific clinical signs. Our results support the need for systematic EHCT in the subgroup of critically ill hemato-oncological patients with AMS.

In our study, we recorded very low scanning rates when compared to published data (4% *vs.* 10.7–33%).[2,3,7,9,12] There are several explanations for this seemingly under-investigation. In contrast to other published studies, we analyzed only EHCTs indicated during ICU stay in oncological patients admitted with non-neurological diagnosis. Namely, we analyzed only EHCTs that were indicated for new neurological signs developed during ICU admission. The high risks associated with transport and CT examination in unstable oncological pa-

tients should be weighed against the benefits in terms of prognosis and therapeutic options.

Complications involving the central nervous system are frequently encountered in critically ill patients. In the literature, when present, they nearly double the risk of ICU mortality (55% *vs*. 28.5% in patients without neurological complications).[13] Similarly, in our study, the outcomes of patients with EHCTs were worse than of patients without brain scans, thus, without neurological impairment.

We found that half of the EHCTs were positive, which was higher than reported by other published retrospective studies (8%–37%).[2,3,7-10] This difference can be explained by the above mentioned study design specificities.

Beyond the number of positive EHCTs, it is worth analyzing their distribution according to clinical indication. The occurrence of FND or seizures is an undisputable EHCT indication. Whether new AMS requires EHCT is debatable. In critically ill patients, AMS is a frequent condition and could indicate an acute intracranial process, but much more commonly is the consequence of systemic conditions (e.g., medications and their interactions, metabolic impairments, sepsis, renal, hepatic, or electrolytic disturbances). Therefore, AMS is probably becoming an important topic in research: two recent studies[8,10] included only patients with AMS, while another two[3,7] found AMS to be the clinical indication in 70% and 88% of cases (though with a lower rate of positive CTs, in 7.5% and 22.8% cases, respectively). Critically ill oncological patients have certain particularities, with sepsis being the most common cause of ICU admission; this increases both the probability of septic encephalopathy and the risk of acute intracranial processes. Hemato-oncology patients are often admitted with severe neutropenia and thrombocytopenia and represent a specific subgroup due to their extremely high risk of septic, hemorrhagic and/or ischemic complications. Brain metastases or leukemic infiltration, which are associated with cerebral oedema, may also be present. These conditions make it difficult to assess the risks and benefits correctly in critically ill haemato-oncological patients. Our data revealed a higher probability of abnormal findings on scans performed for AMS in oncological ICU patients, suggesting that physicians should have a low threshold indicating EHCT for this group.

In the present study, the two main changes identified using CT were acute ischemic and hemorrhagic lesions. While the prevalence of ischemic stroke was comparable with literature data (25–62%)[10,12], the prevalence of hemorrhagic lesions was close to the highest percentage reported (40%).[10,12] Limited published data in critically ill cancer patients indicate that approximately 18%, who underwent brain CT for acute neurologic symptoms and signs, had intracranial hemorrhage.[13]

EHCT and positive EHCT indicated for AMS show similar distribution between hematological and solid tumours. For positive EHCT, the type of newly occurred intracranial processes varies greatly between hematological (mainly hemorrhagic lesions) and solid tumour patients (mainly ischemic lesions). This distribution pattern could be explained by the risk factors mentioned above.

In EHCT studied patients, we recorded a doubled mortality rate compared with the general mortality in ICU patients. However, the mortality rate in positive and negative EHCT patients was similar. In hematological patients, the difference in mortality was recorded between positive and negative EHCT, with higher values for those with AMS as the clinical indication. The mortality of our patients with intracranial hemorrhage was in line with that reported in other studies on critically ill cancer patients (78%)[14] and in hospitalized non-oncological patients (81%).[15,16]

Several limitations of our study should be highlighted. Being a retrospective study, all data were collected from patients' files, which could have led to missed or incomplete information. The cohort size might be considered another limitation, as our study group was smaller than others.[2,3,6,7,9] While the cited studies were conducted on medical, surgical, or mixed ICU patients with or without previous neurological pathology, we included only critically ill oncological patients with new neurological signs occurring during ICU admission. Also, only a fraction of the EHCT performed in our patients were contrast-enhanced due to various contraindications.

Conclusions

In oncological critically ill patients, the diagnostic yield of EHCT is much higher than in other categories of ICU patients. AMS, a clinical sign usually produced by multiple causes, should be a red flag announcing the presence of a new intracranial pathologic process in this specific group of patients. The results of our study support the systematic use of EHCT examination for emerging AMS, as it may identify intracranial complications early, particularly bleeding in hemato-oncological patients.

Author contributions

Conceptualization: Cristian Pristavu, Irina Ristescu, Madalin Manole, Ioana Grigoras. *Data curation:* Cristian Pristavu, Adrian Martin. *Formal analysis:* Cristian Pristavu, Madalin Manole. *Investigation:* Cristian Pristavu. *Methodology:* Cristian Pristavu, Adrian Martin, Irina Ristescu, Emilia Patrascanu, Laura Gavril, Olguta Lungu, Madalin Manole, Ioana Grigoras. *Resources:* Cristian Pristavu. *Software:* Daniel Rusu, Cristian Pristavu. *Supervision:* Ioana Grigoras. *Writing – original draft:* Cristian Pristavu. *Writing-review & editing:* Cristian Pristavu, Adrian Martin, Irina Ristescu, Emilia Patrascanu, Laura Gavril, Olguta Lungu, Madalin Manole, Daniel Rusu, Ioana Grigoras.

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