Presence of Concomitant Systemic Cancer is Not Associated with Worse Functional Long-Term Outcome in Patients with Intracerebral Hemorrhage

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Keywords

Intracerebral hemorrhage · Intracranial hemorrhage · Cancer · Malignancy · Critical care · Prognosis · Imaging

Abstract

Background: Data on clinical characteristics and outcome of patients with intracerebral hemorrhage (ICH) and concomitant systemic cancer disease are very limited. **Methods:** Nine hundred and seventy three consecutive primary ICH patients were analyzed using our prospective institutional registry over a period of 9 years (2006–2014). We compared clinical and radiological parameters as well as outcome – scored using the modified Rankin Scale (mRS) and analyzed in a dichotomized fashion as favorable outcome (mRS = 0–3) and unfavorable outcome (mRS = 4–6) – of ICH patients with and without cancer. Relevant imbalances in baseline clinical and radiological characteristics were adjusted using propensity score (PS) matching. **Results:** Prevalence of systemic cancer among patients with ICH was 8.5% (83/973). ICH patients with cancer were older (77 [70–82] vs. 72 [63–80] years; $p = 0.002$), had more often prior renal dysfunction (19/83 [22.9%] vs. 107/890 [12.0%]; $p = 0.005$), and smaller hemorrhage volumes (10.1 [4.8–24.3] vs. 15.3 [5.4–42.9] mL; $p = 0.017$). After

PS-matching there were no significant differences neither in mortality nor in functional outcome both at 3 months (mortality: 33/81 [40.7%] vs. 55/158 [34.8%]; $p = 0.368$; mRS = 0–3: 28/81 [34.6%] vs. 52/158 [32.9%]; $p = 0.797$) and 12 months (mortality: 39/78 [50.0%] vs. 70/150 [46.7%]; $p = 0.633$; mRS = 0–3: 25/78 [32.1%] vs. 53/150 [35.3%]; $p = 0.620$) among patients with and without concomitant systemic cancer. ICH volume tended to be highest in patients with hematologic malignancy and smallest in urothelial cancer. **Conclusions:** Patients with ICH and concomitant systemic cancer on average are older; however, they show smaller ICH volumes compared to patients without cancer. Yet, mortality and functional outcome is not different in ICH patients with and without cancer. Thus, the clinical history or the de novo diagnosis of concomitant malignancies in ICH patients should not lead to unjustified treatment restrictions.

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Introduction

Cerebrovascular disease is the leading cause of acquired disability [1]. Specifically in Western Countries, alongside with an ageing population, the incidence of

stroke is expected to significantly increase within a few decades [2]. Notably, spontaneous intracerebral hemorrhage (ICH) is related to significant morbidity and mortality [3], harboring implications regarding the socioeconomic burden related to functional long-term outcome [1].

Besides vascular diseases, cancer represents the major cause for death worldwide [4]. Also linked to age, both population-based incidence and prevalence rates of cancer will likewise increase [5]. Given several selfsame risk factors related to stroke and cancer, both diseases may affect patients concomitantly [6–8]. Yet, there are very limited data – all with substantial methodological shortcomings [9–11] – on the interaction between ICH and cancer in relation to functional outcome.

Intuitively, stroke physicians would prognosticate the functional outcome to be worse in those ICH patients with concomitant cancer diagnoses [12]. However, a solid clinical study – with a sound statistical approach accounting for imbalances in baseline parameters – is missing.

This study (i) investigated the prevalence of concomitant systemic cancer disease among patients with ICH, (ii) assessed clinical and radiological characteristics of ICH cancer-patients, and (iii) explored the clinical relevance of coincidental cancer regarding functional long-term outcome after ICH.

Methods

Patient Selection

All consecutive patients with ICH admitted to the Department of Neurology, University Hospital Erlangen, Germany, over a period of 9 years (2006–2014) were prospectively entered into our institutional registry ($n = 1,134$). For this observational study, we excluded 161 patients because of secondary ICH etiologies ($n = 112$; for example, trauma, aneurysm, intratumoral hemorrhage, or arteriovenous malformation), missing data ($n = 36$), and refused consent ($n = 13$). The study was approved by the institutional review board and informed consent of the patients or legal representatives was obtained.

Data Acquisition

Demographics (age, gender), preexisting status (modified Rankin Scale [mRS] [13] prior to ICH, comorbidities), medication, admission status (blood pressure, Glasgow Coma Scale, National Institutes of Health Stroke Scale [NIHSS], and ICH Score), in-hospital parameters (length of stay, in-hospital mortality, incidence of pneumonia, sepsis, mechanical ventilation and placement of external ventricular drainage) as well as laboratory data (international normalized ratio [INR], activated partial thromboplastin time, count of leucocytes/thrombocytes, hemoglobin, C-reactive protein, creatinine, troponin) were retrieved from medical records

and institutional databases. Liver dysfunction (chronic hepatic disease or Bilirubin $>2\times$ or AST/ALT/AP $>3\times$ upper limit of normal) and renal dysfunction (glomerular filtration rate <60 mL/min/ 1.73 m 2) were defined according to international criteria [14, 15]. We retrospectively reviewed the medical charts of all included 973 ICH patients for diagnosis of at least one malignant cancer. In patients with more than one cancer type, we scored the cancer type that – according to international criteria (National Comprehensive Cancer Network Guidelines) – was graded as more malignant with shorter survival times [9, 11]. Active cancer was defined as diagnosed or treated within the previous 6 months or reported as recurrent/metastatic cancer, while other malignancies were defined as nonactive [16]. The type of treatment (operation/radio-/chemotherapy) and the period between the time that the tumor was diagnosed and the onset time of ICH were assessed.

Outcome Measurement

Mortality and functional outcome (dichotomized into favorable outcome, defined as mRS between 0 and 3, and unfavorable outcome, mRS = 4–6, as described previously in randomized ICH trials [17, 18]) were evaluated at 3 months (short-term outcome) and at 12 months (long-term outcome) after ICH onset and were obtained by physicians trained and certified for outcome evaluation [19]. The assessment tool was a standardized mailed questionnaire; if the questionnaire was not returned within 4 weeks, then a semi-structured telephone interview was conducted.

Imaging

ICH was diagnosed by multislice computed tomography (SOMATOM Volume Zoom or SOMATOM Definition AS+; Siemens Healthcare, Forchheim, Germany) or 1.5 Tesla magnetic resonance imaging (MAGNETOM Sonata or MAGNETOM Aera; Siemens Healthcare, Erlangen, Germany). Two neuroradiologists – blinded to clinical data – independently evaluated initial and follow-up imaging, including eventual MRI during the follow-up period performed to exclude secondary ICH etiology after ICH resection. Patients with intracranial lesions were included only if imaging showed hemorrhage in a brain area topographically distant to the tumorous lesion. ICH volume was assessed using the ABC/2 formula [20] or the ABC/3 formula [21] and adjusted to imaging modalities [22]. Hematoma enlargement was defined as a relative volume increase of more than 33% from initial to follow-up imaging [23]. The site of hemorrhage and ventricular involvement were scored as described earlier [24].

Statistical Analysis

Data were analyzed using SPSS version 20.0 (SPSS Inc) and R version 2.12.0 (R project). We performed 2-sided statistical tests and set the significance level at $\alpha = 0.05$. Frequency distribution of categorical variables (presented as total number and frequency in brackets) was compared by Pearson's χ^2 and the Fisher's exact test. Data of continuous variables (presented as median and interquartile range because of non-normally distributed) were analyzed using the Mann-Whitney U test. A total of 16 patients were excluded from outcome analysis only as there were no follow-up information on outcome measures available (ICH with cancer: 2/83 [2.4%] after 3 months and 5/83 [6.0%] after 12 months; ICH without cancer: 3/161 [1.9%] after 3 months and 11/161 [6.8%] after 12 months). Online supplementary Table 1 (for all online suppl. material, see www.karger.com/doi/10.1159/000479075)

displays the baseline characteristics of these patients who were lost to follow-up. To properly compare the functional outcome of ICH patients with and without cancer, we performed a propensity score (PS) matching using a balanced, parallel, 1:1 ratio nearest-neighbor approach [25]. We adjusted for relevant imbalances of baseline parameters relating to demographics, comorbidities, admission status, and radiological ICH characteristics (i.e., $p < 0.10$) [26].

Results

Prevalence of Cancer and Baseline Characteristics

Overall, of the 973 included patients with ICH, 83 patients (8.5%) had a diagnosis of at least one type of cancer (Table 1). ICH patients with cancer were older (77 [70–82] vs. 72 [63–80] years; $p = 0.002$), and had more often preexisting renal dysfunction (19/83 [22.9%] vs. 107/890 [12.0%], $p = 0.005$) with correspondingly higher creatinine levels at admission (90.17 [65.86–113.15] vs. 77.79 [63.65–95.69] $\mu\text{mol/L}$; $p = 0.006$). As compared to patients without cancer, those with concomitant cancer diagnoses showed smaller ICH volumes (10.1 [4.8–24.3] vs. 15.3 [5.4–42.9] mL; $p = 0.017$). Notably, the clinical admission status was comparable and there were no other significant differences in comorbidities, admission status, complications during hospital stay, or hematoma characteristics (Table 1). Patients with active cancer also showed more pre-existing renal dysfunction, but presented more frequently with liver dysfunction and higher C-reactive protein levels on admission (online suppl. Table 2).

Cancer-Associated Parameters

Among ICH patients with cancer, more than 30 cancer types were evident (Table 2), categorized into solid tumors (71/83; 85.5%), primary brain tumors (2/83; 2.4%), and hematologic malignancies (10/83; 12.0%). An active cancer was present in 29 out of 83 (34.9%), and 8 out of 83 (9.6%) showed systemic metastases. The median time from cancer diagnosis to ICH was 62 months (1,865 days [537–4,668]). Out of 83 ICH cancer-patients, 26 (31.3%) received prior chemotherapy, 21 (25.3%) received radiotherapy, and 66 (79.5%) underwent tumor surgery.

ICH volume tended to be the highest in patients with hematologic malignancies (26.5 [6.4–44.6] vs. 9.5 [4.7–21.9] mL; $p = 0.166$) and smallest with urothelial cancer (1.0 [0.6–13.8] vs. 10.5 [5.4–27.8] mL; $p = 0.076$). Colorectal cancer patients had larger ICH volumes (20.9 [10.9–100.8] vs. 9.3 [4.0–21.8] mL; $p = 0.012$) compared to patients with other cancer types. After exclusion of an-

ticoagulated patients, colorectal cancer patients still presented with larger ICH volumes (14.3 [8.0–39.4] vs. 6.7 [2.4–13.6] mL; $p = 0.015$), higher ICH scores (2 [2–4] vs. 1 [0–3]; $p = 0.035$) and higher INR values (1.14 [1.03–1.31] vs. 1.01 [0.97–1.09]; $p = 0.032$). Urothelial cancer patients had more often a prior ischemic stroke (4/5 [80.0%] vs. 14/78 [17.9%], $p = 0.007$).

Outcome of ICH Patients with Systemic Cancer

In the unadjusted analysis (Table 1), ICH patients with and without cancer showed no significant differences in mortality, or short- and long-term outcome. To account for confounders in baseline characteristics (age, gender, renal dysfunction, ICH volume, and NIHSS; Table 1), we performed PS matching, after which the PS-matched cohorts were evenly balanced in terms of demographics, comorbidities, admission status, and ICH volume (online suppl. Table 3).

Functional outcome data at discharge, at 3 months, and at 12 months are provided in Figure 1. Regarding mortality, there were no significant differences in the proportion of patients with in-hospital mortality (18/83 [21.7%] vs. 36/161 [22.4%]; $p = 0.904$), short-term mortality (33/81 [40.7%] vs. 55/158 [34.8%]; $p = 0.368$), and long-term mortality (39/78 [50.0%] vs. 70/150 [46.7%]; $p = 0.633$). Among ICH patients with and without cancer, there were no significant differences in the proportion of patients with favorable outcome at discharge (mRS = 0–3: 18/83 [21.7%] vs. 41/161 [25.5%]; $p = 0.514$), at 3 months (mRS = 0–3: 28/81 [34.6%] vs. 52/158 [32.9%]; $p = 0.797$) and at 12 months (mRS = 0–3: 25/78 [32.1%] vs. 53/150 [35.3%]; $p = 0.620$).

Kaplan-Meier survival curves are provided in Figure 2. Mortality analysis over a 12-month follow-up period by Log Rank ($p = 0.724$), Breslow ($p = 0.832$), and Tarone-Ware ($p = 0.776$) testing showed no significant difference in mortality between propensity-score-matched ICH patients with and without cancer (Fig. 2). Sub-analysis of ICH cancer-patients with active versus non-active cancer (online suppl. Fig. 1, 2) and also sub-analysis of deep and lobar ICH location for patients with and without cancer (online suppl. Fig. 3, 4) revealed no significant differences in mortality or functional outcome.

Discussion

This study for the first time thoroughly analyzed the prevalence, types, and clinical characteristics of concomitant cancer diseases in a large cohort of ICH patients. We

Table 1. Admission, in-hospital, and outcome characteristics of ICH patients with and without cancer

Overall patients with ICH (<i>n</i> = 973)	ICH without cancer (<i>n</i> = 890)	ICH with cancer (<i>n</i> = 83)	<i>p</i> value
Age, years	72 (63–80)	77 (70–82)	0.002
Gender, female	419 (47.1)	30 (36.1)	0.056
Prior comorbidities			
Premorbid mRS	1 (0–2)	1 (0–2)	0.469
Hypertension	730 (82.0)	70 (84.3)	0.598
Diabetes mellitus	239 (26.9)	22 (26.5)	0.945
Renal impairment	107 (12.0)	19 (22.9)	0.005
Liver impairment	48 (5.4)	8 (9.6)	0.112
Prior ischemic stroke	153 (17.2)	18 (21.7)	0.303
Prior hemorrhagic stroke	82 (9.2)	6 (7.2)	0.547
Antiplatelet medication	272 (30.6)	22 (26.5)	0.442
Oral anticoagulation	186 (20.9)	19 (22.9)	0.670
Admission status			
Glasgow Coma Scale	13 (5–15)	13 (10–15)	0.137
NIHSS	14 (5–26)	11 (4–19)	0.054
ICH score	2 (1–3)	1 (0–3)	0.203
Imaging characteristics			
Initial ICH volume, mL	15.3 (5.4–42.9)	10.1 (4.8–24.3)	0.017
Intraventricular hemorrhage	433 (48.7)	41 (49.4)	0.897
Deep	419 (47.1)	37 (44.6)	0.662
Lobar	393 (44.2)	40 (48.2)	0.479
Cerebellar	62 (7.0)	6 (7.2)	0.928
Brainstem	50 (5.6)	2 (2.4)	0.307
Hematoma growth	80 (9.0)	9 (10.8)	0.575
Time from first to follow-up imaging, h	21.0 (13.0–30.0)	23.0 (16.0–35.5)	0.310
Initial laboratory values			
Thrombocytes, 10 ³ /μL	222.00 (182.00–268.50)	216.50 (156.75–267.50)	0.552
Leucocytes, 10 ³ /μL	9.07 (7.07–11.64)	8.18 (6.18–11.29)	0.115
CRP, nmol/L	380.96 (133.34–933.35)	390.48 (161.91–780.97)	0.862
Creatinine, μmol/L	77.79 (63.65–95.69)	90.17 (65.86–113.15)	0.006
Troponin, ng/mL	0.02 (0.01–0.03)	0.01 (0.01–0.04)	0.578
Clinical parameters during hospital stay			
Length of stay, day	10.0 (5.0–17.0)	10.0 (6.0–16.0)	0.713
MAP at admission, mm Hg	116.6 (100.3–133.3)	114.0 (103.3–132.0)	0.977
Mechanical ventilation	380 (42.7)	27 (32.5)	0.073
External ventricular drain	251 (28.2)	21 (25.3)	0.573
Complications			
Sepsis	160 (18.0)	19 (22.9)	0.269
Pneumonia	306 (34.4)	29 (34.9)	0.919
Urinary tract infection	83 (9.3)	6 (7.2)	0.526
Outcome			
In-hospital mortality	213 (23.9)	18 (21.7)	0.646
mRS 3 months 0–3	289/872 (33.1)	28/81 (34.6)	0.794
mRS 12 months 0–3	287/813 (35.3)	25/78 (32.1)	0.565
1-Year mortality	358/813 (44.0)	39/78 (50.0)	0.311

Values are median (IQR) or *n* (%).

IQR, interquartile range; mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale; ICH, intracerebral hemorrhage; hematoma growth defined as volume increase >33% on follow-up imaging; INR, international normalized ratio; aPTT, activated partial thromboplastin time; CRP, C-reactive protein; MAP, mean arterial pressure.

Table 2. Cancer and admission characteristics of cancer types

	Overall ICH patients with cancer (n = 83)	Hemato- oncologic malignancy (n = 10)	Primary brain tumor (n = 2)	Solid tumor (n = 71)	Colorectal (n = 11)	Prostate (n = 11)	Renal (n = 10)	Breast (n = 7)	Skin (n = 8)	Urothelial (n = 5)	Other (n = 19)
Cancer characteristics											
Active cancer	29 (34.9)	8 (80)	1 (50)	20 (28.2)	0 (0)	2 (18.2)	2 (20)	2 (28.6)	2 (25)	2 (40)	10 (52.6)
Systemic metastases	8 (9.6)	2 (20)	0 (0)	6 (8.5)	0 (0)	2 (18.2)	1 (10)	0 (0)	0 (0)	0 (0)	3 (15.8)
Time cancer diagnosis to ICH, days	1,865 (537–4,668)	365 (25–4,764)	1,054 (48–1,054)	1,923 (882–4,749)	4,668 (2,915–6,000)	1,445 (882–2,388)	1,446 (992–2,890)	5,460 (1,887–7,064)	1,489 (339–30,914)	2,945 (717–9,557)	890 (206–3,001)
Chemotherapy	26 (31.3)	4 (40)	1 (50)	21 (29.6)	4 (36.4)	4 (36.4)	2 (20)	4 (57.1)	1 (12.5)	1 (20)	5 (26.3)
Radiotherapy	21 (25.3)	3 (30)	1 (50)	17 (23.9)	3 (27.3)	5 (45.5)	0 (0)	3 (42.9)	0 (0)	0 (0)	6 (31.6)
Operation	66 (79.5)	3 (30)	0 (0)	63 (88.7)	10 (90.9)	6 (54.5)	10 (100)	7 (100)	7 (87.5)	5 (100)	18 (94.7)
Admission characteristics											
Age, years	77 (70–82)	76 (64–78)	71 (59–71)	77 (71–82)	79 (74–85)	80 (77–85)	75 (58–82)	74 (72–85)	82 (76–86)	77 (72–79)	71 (57–78)
Gender, female	30 (36.1)	4 (40)	1 (50)	25 (35.2)	4 (36.4)	0 (0)	0 (0)	7 (100)	3 (37.5)	0 (0)	11 (57.9)
Premorbid mRS	1 (0–2)	0 (0–2)	2 (1–2)	1 (0–2)	1 (0–2)	0 (0–3)	1 (0–2)	1 (0–3)	1 (0–3)	1 (0–3)	1 (0–2)
Prior stroke	24 (28.9)	2 (20)	2 (100)	20 (28.2)	3 (27.3)	4 (36.4)	2 (20)	1 (14.3)	0 (0)	5 (100)	5 (26.3)
Oral anticoagulation	19 (22.9)	2 (20)	1 (50)	16 (22.5)	3 (27.3)	2 (18.2)	5 (50)	0 (0)	1 (12.5)	1 (20)	4 (21.1)
MAP at admission, mm Hg	114.0 (103.3–132.0)	123.3 (100.0–123.3)	50.0 (50.0–50.0)	114.0 (104.0–137.0)	109.3 (91.1–136.5)	121.0 (114.8–134.8)	127.0 (109.5–143.0)	104.0 (104.0–104.0)	124.0 (120.0–124.0)	142.8 (112.5–142.8)	104.7 (93.3–114.0)
Initial ICH volume, mL	10.1 (4.8–24.3)	26.5 (6.4–44.6)	22.7 (0.4–22.7)	9.5 (4.8–20.9)	20.9 (10.9–100.8)	10.0 (2.0–24.3)	6.9 (5.3–16.7)	6.6 (3.2–28.0)	13.3 (3.2–21.8)	1.0 (0.6–13.8)	9.5 (6.6–14.3)
Intraventricular hemorrhage	41 (49.4)	5 (50)	1 (50)	35 (49.3)	6 (54.5)	8 (72.7)	6 (60)	1 (14.3)	2 (25)	1 (20)	11 (57.9)
ICH score	1 (0–3)	3 (1–4)	3 (0–3)	1 (0–3)	3 (2–5)	3 (2–4)	1 (0–3)	1 (1–1)	1 (0–3)	0 (0–1)	1 (0–3)
INR	1.04 (0.98–1.22)	1.07 (1.02–1.16)	1.11 (0.98–1.11)	1.04 (0.98–1.23)	1.23 (1.04–2.08)	1.12 (1.01–1.22)	1.04 (0.97–1.52)	0.98 (0.96–1.01)	1.01 (0.97–1.06)	1.05 (0.97–1.18)	0.99 (0.96–1.25)
Thrombocytes, 10 ³ /μL	216.50 (156.75–267.50)	204.00 (132.00–243.00)	276.50 (237.00–276.50)	217.50 (156.00–272.25)	202.00 (154.00–252.00)	217.00 (147.00–258.00)	206.00 (162.25–272.25)	266.00 (169.00–348.00)	179.00 (140.00–203.00)	280.00 (139.50–481.00)	257.00 (170.00–333.00)

Values are median (IQR) or n (%).

Active cancer defined as diagnosed or treated within the previous 6 months or reported as recurrent/metastatic cancer [16]; ICH, intracerebral hemorrhage; IQR, interquartile range; mRS, modified Rankin Scale; MAP, mean arterial pressure; INR, international normalized ratio.

Fig. 1. Distribution of functional outcome (modified Rankin Scale) of ICH patients with cancer and PS-matched (age, gender, prior renal failure, NIHSS, ICH volume and ventilation) cohort without cancer. **a** Discharge outcome; **b** Short-term outcome (3 months); **c** Long-term outcome (12 months); mRS = modified Rankin score; scale: 0–6; from no deficit to death. The difference between favorable (mRS = 0–3) and unfavorable (mRS = 4–6) functional outcome is illustrated by a bold line and p values are provided for comparison of patients with and without cancer.

Fig. 2. Kaplan-Meier survival curve from index ICH until 1-year follow-up in patients with cancer ($n = 83$) and PS-matched (age, gender, prior renal failure, NIHSS, ICH volume and ventilation) cohort without cancer ($n = 161$).

verified that ICH patients with concomitant cancer were older; however, we also showed smaller ICH volumes resulting in similar rates of mortality and unfavorable functional outcome compared to ICH patients without cancer. Using PS-matching, we demonstrated that both mortality and functional outcome do not significantly differ among ICH patients with and without cancer over a period of 12 months after ICH. Two important aspects deserve attention.

First, while it is not surprising that ICH patients with cancer were older than ICH patients without cancer [5], the fact that ICH volumes are smaller in concomitant cancer is novel. The complex interaction with the coagulation system and a prothrombotic status, evident up to many years after cancer diagnosis [27], represents a possible pathophysiological explanation [28, 29]. In line with this consideration, urothelial cancer patients in our study tended to have smaller ICH volumes consistent with previous studies demonstrating an increased risk of thrombotic events based on a prothrombotic status [27]. Further supportive, colorectal cancer patients showed larger ICH volumes, a finding that is possibly linked to surgery-based, impaired vitamin-K metabolism resulting in higher INR values [30, 31]. This aspect draws specific attention to optimally handle coagulation measures in the acute phase of ICH in colorectal cancer patients to minimize risk of hematoma enlargement [24].

Second, as demonstrated here, functional long-term outcome after ICH is not significantly impacted by concomitant cancer diagnosis. This finding harbors a significant clinical implication, as stroke physicians usually negatively stigmatize ICH patients with concomitant cancer. This intuitive feeling was recently supported by a registry database study reporting on higher mortality and less favorable outcome of ICH cancer patients at the time of hospital discharge [11]. However, this study was solely based on diagnosis codes and lacked most relevant clinical data (Glasgow Coma Scale, NIHSS, ICH volume, cancer details). Further significant shortcomings that – in the opinion of the authors of this study – undermine the conclusion of the manuscript refer to insufficient statistical corrections for imbalances of baseline characteristics [11]. In fact, our present study establishes no differences regarding both mortality and functional outcome over a one-year follow-up period among ICH patients with and without concomitant cancer. After adjusting for imbalances in baseline characteristics, ICH patients with cancer were more frequently affected by sepsis. Yet accounting for sepsis would rather benefit the cancer patient

group and this therefore supports the conclusion of our study. A possible reason why an additional cancer diagnosis does not impact long-term prognosis after ICH relates to the severity of the bleeding itself, as demonstrated previously [3, 24, 32–34]. Therefore, the intuitive prognostication that ICH patients with cancer show worse outcomes needs a strong counterbalance to avoid early treatment restrictions and thus self-fulfilling prophecies [12, 35].

This study has certain strengths, such as the large sample size with reliable clinical data and a prospectively assessed 12 months follow-up period as well as the status of our department as a neurovascular care center including ICH patients with and without cancer in the hospital catchment area. Nevertheless, this is a single-center study. The numbers of patients with specific cancer types were limited; hence, conclusions from sub-analyses and multiple comparisons leave room for controversy. Further, on the one hand, end-stage palliative cancer patients treated at Oncology Departments or hospices and receiving comfort care only may have been missed out by our selection approach. On the other hand, in our included patients, we did not apply a standardized cancer-screening protocol for occult cancer and that is why some cancer patients potentially were missed, resulting in residual selection bias. Considering ICH etiology, there were no fixed time points for MRI imaging after ICH resorption and stroke recurrence was not assessed due to our study design. Yet, given the equal distribution of functional outcome and mortality over the one-year follow-up including sub-analysis for ICH location, no essential imbalances ought to be present among both groups. Finally, we approached the field by studying all ICH patients and their eventual cancer co-diagnosis, instead of investigating ICH incidence among all cancer patients at our center, and that is why we do not have those patients as reference.

In conclusion, our study indicates that there are no relevant differences between ICH patients with and without cancer in terms of mortality and functional outcome. This finding may help physicians in the clinical management of ICH by avoiding unjustified care restrictions in ICH patients with concomitant cancer.

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Disclosure Statement

The authors have no conflicts of interest to disclose.

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Author Contribution

M.I.S. and H.B.H. designed the study and wrote the manuscript. M.I.S., J.A.S., J.H., A.G.-J., D.M., and V.D.B. obtained clinical data by reviewing institutional databases and the patients' medical charts. P.H., H.L., and T.S. obtained and analyzed radiological data. S.T.G. and J.B.K. obtained functional outcome data and performed statistical analyses. S.S. critically revised the manuscript. All authors have read the manuscript, agreed with the contents, and approved of the final version of the manuscript.

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