Risks for intracranial hemorrhage in patients with glioblastoma or brain metastases and atrial fibrillation with and without anticoagulation

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Background

Whilst previous studies found an increased risk of bleeding for patients with glioma (1,2) under anticoagulation (AC), there was no difference reported for patients with brain metastases (3). The aim of this study was to assess this risk in the context of AC for atrial fibrillation (AF) to prevent stroke.

Methods

Our institution’s database (from 2006 to 2016) was screened for patients with GBM or BM and AF with an indication for prophylactic anticoagulation according to their CHA2DS2-VASc-Score (≥ 2). AC was either performed with heparins, phenprocoumon or novel oral anticoagulants (NOAC). Applying the propensity score method, patient cohorts (matched according to primary tumor, age, sex, therapy) were generated (GBM [or BM] with AF+/-AC, GBM [or BM] without AF/AC, no GBM [or BM] but AF on AC). ICH was defined as any new blood on imaging and categorized according to symptoms and local vs. space occupying appearance (Figure 1). A logistic mixed effects model was calculated to compare the risk for ICH between the groups.

Table 1. Descriptive Statistics

Variable	GBM+AF (n=74)	GBM-AC (n=74)	Variable	BM+AF (n=45)	BM-AC (N=45)
median age (range)	70.9 (35-83)	71.5 (25-91)		68.4 (40-81)	68 (42-83)
sex (male/female)	70.3%/29.7%	74.3%/25.7%		62.2%/37.8%	53.3%/46.7%
resection					
biopsy	22 (29.7%)	25 (33.8%)	yes	24 (53.3%)	18 (40.0%)
subtotal	21 (28.4%)	18 (24.3%)	no	21 (46.7%)	27 (60.0%)
total	31 (41.9%)	31 (41.9%)			
adjuvant therapy					
Stupp	57 (77.0%)	56 (75.7%)	Chemo	33 (73.3%)	34 (75.6%)
Stupp+Avastin	16 (21.6%)	17 (23.0%)	Chemo+RT	10 (22.2%)	9 (20.0%)
Palliative	1 (1.4%)	1 (1.4%)	RT alone	2 (4.4%)	2 (4.4%)
anticoagulation					
NOAC	15 (20.2%)	none		8 (17.7%)	none
Phenprocoumon	5 (8.2%)			4 (9%)	
Heparin	45 (60.8%)			24 (53.3%)	
none	13 (17.5%)			9 (20%)	
ICH					
yes	10 (13.5%)	8 (10.8%)		7 (15.6%)	7 (15.6%)
no	64 (86.5%)	64 (89.2%)		38 (84.4%)	48 (84.4%)
extend of bleed					
[microbleeds	0	2 (20.0%)		1 (11.1%)	7 (50.0%)]
local	3 (30.0%)	7 (70.0%)		4 (44.4%)	7 (50.0%)
Space-occupying	7 (70.0%)	1 (10.0%)		3 (33.3%)	0
extracranial	0	0		1 (11.1%)	0
localisation					
parenchymal	6 (60.0%)	6 (60.0%)		8 (100.0%)	13 (92.9%)
subdural	3 (30.0%)	4 (40.0%)		0	1 (7.1%)
other	1 (10.0%)	0		0	0
clinical presentation					
silent	4 (40.0%)	7 (70.0%)		4 (44.4%)	10 (71.4%)
symptomatic	6 (60.0%)	3 (30.0%)		5 (55.6%)	4 (28.6%)
primary tumor					
Lung				23 (51.1%)	29 (64.4%)
Breast				8 (17.8%)	9 (20.0%)
Melanoma				3 (6.7%)	4 (9%)
other				11 (24.4%)	3 (6.6%)

Table 2. Mixed Effects Logistic Regression after matching patients with brain tumor on anticoagulation to patients with brain tumor without anticoagulation

	Est	LL	UL	std. error	p-value
Group GBM+AF vs. GBM-AC (N=74)	-0.254	-1.245	0.737	0.506	0.616
age	0.003	-0.046	0.051	0.025	0.91
sex	-0.725	-2.021	0.571	0.661	0.273
Group BM+AF vs. BM-AC (N=45)	0	-1.14	1.14	0.582	1
age	-0.017	-0.082	0.047	0.033	0.596
sex	0.031	-1.122	1.183	0.588	0.958

AC=anticoagulation, AF=atrial fibrillation, BM=brain metastasis, GBM=glioblastoma, ICH=intracranial hemorrhage, NOAC=novel oral anticoagulant, RT=radiotherapy, Stupp=Temozolomide plus RT

Conclusion

Only 2/3 of patients with AF were anticoagulated. ICHs occurred most in patients with BM, there was no association with AC in any group. Although the cohorts might be too small to detect significance in logistic regression, patients with GBM on AC had more ICHs compared to the controls.

Figure 1. A) Localized bleeding in a left cerebellar metastasis of a 64-year old male (lung cancer, on Rivaroxaban) presenting with a deterioration of gait. B) Space occupying ICH in a 64-year-old with lung cancer and on phenprocoumon for atrial fibrillation. He presented with a right hemiparesis and somnolence (INR on admission 5.5).

Results

In total 174 patients were identified of which 74 with GBM (62% on AC) and 45 with BM (62% on AC) were matched. ICH occurred in 13,5% of GBM+AF and in 10.8% of GBM-AC, whereas 6% of patients with AF on AC suffered ICH (follow-up median 8 months). In both BM groups, 15.6% of patients had ICHs, whereas 7% with AF on AC had ICHs (follow-up median 5,5 months). Adding the vascular control group (AF on AC) to the mixed effects logistic regression reduced the cohort to 48 matched patients with GBM and 38 matched patients with BM. There was still no significant difference in the incidence of ICH for the variables of group, age and sex in either regression.

References:
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