Real life cost of treatment and follow-up of patients with glioblastoma in Belgium: a retrospective patient chart review

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SUMMARY

We calculated the management costs from diagnosis to death of glioblastoma patients treated at the Antwerp University Hospital between 2007 and 2016. Overall, the average cost per patient from the health care payer's perspective was €45,165 (95% confidence interval €37,204-€54,104). The major cost driving factor was hospitalisation.

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INTRODUCTION

Glioblastoma (GBM) or grade IV glioma is the most common primary malignant tumour of the central nervous system (CNS). GBM is a poorly differentiated and highly invasive tumour but generally does not metastasise outside the CNS. Overall, GBM is a disease of older age, but it can occur in patients of any age. Exposure to ionising radiation is the only known risk factor for the development of GBM. Optimal treatment of GBM for fit patients consists of surgical resection followed by concomitant chemoradiation with temozolomide followed by adjuvant temozolomide (Stupp regimen).[1,2] Despite proper treatment, patients with GBM have a poor prognosis. According to the Belgian Cancer Registry, the five-year survival rates are 4.7% in males and 6.2% in females.[3] Cancer treatment is associated with considerable costs for patient and society. This study aimed to estimate the management-related direct costs of GBM in a real life setting both from the perspective of the Belgian National Institute for Health and Disability Insurance (NIHDI) and the patient. In a time of tight budgets, physicians should be aware of the disease- and treatment-related costs.

MATERIAL AND METHODS

STUDY DESIGN

An observational and retrospective patient chart review was conducted at the Antwerp University Hospital (UZA), evaluating real-life resource use associated with the inpatient and outpatient management of patients with GBM, from diagnosis to death. Information regarding resource use was obtained using the patient's medical hospital file. Outpatient and inpatient resource use at the UZA was collected in a similar way. Outpatient resource use outside the UZA (for example, visits to a general practitioner) was not collected. An exception was made for prescribed medication after hospitalisation.

Descriptive statistics were used to present the demographic and clinical patient characteristics. Healthcare costs were calculated as follows. Quantities of resources were collected from patient records during the chart abstraction. The quantity of

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TABLE 1. Demographic and disease characteristics, n: number of patients.

Demographic and disease characteristics	n=51
Median age, years (range)	60.0 (5.0-86.0)
Male/Female, n	31/20
Hemisphere involved, n (% of total)	
Right	28 (54.9%)
Left	20 (39.2%)
Median	3 (5.9%)
Location of disease, n (% of total)	
Frontal	15 (29.4%)
Temporal	13 (25.5%)
Parietal	9 (17.6%)
Occipital	1 (2.0%)
Other	13 (25.5%)
Management	
Surgery alone	16 (31.4%)
Stupp regimen	24 (47.1%)
Others	11 (21.5%)
Type of surgery	
Surgical resection	37 (72.5%)
Biopsy	14 (27.4%)

resources was then multiplied by the unit costs to calculate a cost per patient from the health care payer's perspective and the patient's financial contribution or co-payment for the entire study period. Unit costs (costs for the purpose of cost comparability) were obtained through official cost listings published by the NIHDI, actualised to March 2017. The average cost was calculated, and the 95% confidence intervals (CI) were reported using bootstrap techniques. Approval by the hospital's ethics committee was obtained before the start of the data collection. Informed consent was not required as only deceased patients were included in this study.

PATIENT SELECTION

The Cancer Registry department of the UZA prepared a list of all GBM patients diagnosed between 2007 and 2016 using multidisciplinary oncologic consult (MOC) reporting and the Pathology Department register. Eligible for the chart review were patients with new histological diagnosis of GBM between 2007 and 2016, who died before the time of the patient chart review (August 2016) and for whom information regarding resource use was available at the UZA from diagnosis to death. Excluded were patients with incomplete follow-up at the UZA. Follow-up was considered incomplete if the patient did not receive its complete treatment course at the UZA, with the exception of radiotherapy when administered at an affiliated hospital. Patient data were collected from the patient's medical file and inserted anonymously in an electronic case report. For each patient, demographic and disease-related data were collected. Quantities of resource use were collected per patient for each treatment line.

RESULTS

PATIENT CHARACTERISTICS

Between 2007 and 2016, 171 tumour specimens revealed a diagnosis of GBM, including 69 tumour specimens sent to the UZA Pathology Department of patients treated at other centres. From the remaining 102 patients, six were alive at the time of the chart review and one patient had been diagnosed with recurrent disease. The diagnosis was not histologically confirmed in one patient and another patient was also treated for another neoplastic disease during the disease course of glioblastoma. The follow-up at the UZA was incomplete in 42 patients. Fifty-one patients (31 male, 20 female) were included in the analysis. Patient and disease characteristics are summarised in *Table 1*.

TABLE 2. Resource use: procedures, tests and visits.

	N=51 (%)	n
Inpatient resource use		
Lab tests	51 (100%)	12.8
CT scans	50 (98%)	3.1
X-ray	49 (96%)	5.9
Ultrasound	16 (31%)	0.6
MRI	47 (92%)	2.4
ECG	45 (88%)	2.4
Other tests	30 (59)	0.9
Outpatient resource use		
Lab tests	37 (73%)	13.5
CT scans	15 (29%)	0.5
X-ray	14 (27%)	0.4
Ultrasound	9 (18%)	0.3
MRI	35 (69%)	3.7
ECG	12 (24%)	0.4
Other tests	11 (22%)	0.4
Oncology visits	28 (55%)	8.2
Neurology visits	16 (31%)	0.6
Neuro-surgery visits	26 (51%)	1.2
Radiotherapy visits	31 (61%)	17.5
Other visits	24 (47%)	1.7

N (%): number (%) of patients with tests/visits, n: average number of tests/visits per patient, CT: computed tomography, MRI: magnetic resonance imaging, ECG: electrocardiography.

MEDICAL MANAGEMENT

A complete or partial surgical resection was performed in 37 patients (73%); a biopsy without surgical resection in 14 (27%). Twenty-five patients (49%) received chemotherapy for GBM including concomitant chemoradiation (n=22), temozolomide monotherapy (n=16), bevacizumab (n=2) and other (n=1).

OUTCOME

Median overall survival (OS) was 9.3 months (range 0.1-42.6 months). In patients treated with surgery alone (n=16), either resection or biopsy, the median OS was 1.6 months (range 0.1-14.9). The median OS in patients treated with the Stupp regimen (n=24) was 14.3 months (range 3.4-42.6). In patients treated with another treatment (n=11) regimen, the median OS was 10.1 months (range 1.1-35.1 months). The cause of death was progressive disease in 44 patients (86.3%), euthanasia in 2 (3.9%), pneumonia in 1 (2.0%) and unknown in 4 (7.8%).

RESOURCE USE

All patients were hospitalised at least once. The average number of hospitalisations per patient was 2.5 (standard deviation [SD] 1.5), the average length of stay was 16.3 days (SD 14.9). The reasons for hospitalisation included surgery (47%), diagnostic work-out (33%) and deterioration of the general condition (29%). Surgical procedures (n=98) included surgical resection (n=48), biopsy (n=13) and other (i.e., brain ventricle drain placement, port catheter placement and laminectomy; n=9). The resource use is summarised in *Table 2*.

Sixteen patients (32%) received treatment for recurrent disease including surgery (n=8) and chemotherapy (n=8). All patients received concomitant drugs, including corticosteroids

TABLE 3. Costs; 95% confidence interval (95% CI).

Costs	Number of patients	Median survival time in months (range)	Cost public payer's perspective, mean (95% CI)	Cost public payer's perspective per month	Cost patient's perspective, mean (95% CI)	Cost patient's perspective per month	Average total cost (95% CI)
Surgery alone	16	1.6 (0.1-14.9)	€32,723 (€24,556-€41,600)	€11,125	€1,013 (€856-€1612)	€344	€33,736 (€25,356-€42,913)
Stupp regimen	24	14.3 (3.4-42.6)	€56,758 (€43,287-€71,879)	€3,400	€1,672 (€1,351-€2,005)	€100	€58,429 (€44,719-€73,564)
Other	11	10.1 (1.1-35.1)	€31,556 (€21,917-€42,399)	€2,637	€1,291 (€852-€1,750)	€65	€32,847 (€22,800-€44,048)
Overall	51	9.3 (0.1-42.6)	€43,782 (€35,878-€52,441)	€3,919	€1,383 (€1,175-€1,603)	€124	€45,165 (€37,204-€54,104)

(n=51), analgesics (n=51), anti-thrombotics (n=49), intravenous fluids (n=47), laxatives (n=39), gastric acid inhibitors (n=36), anti-epileptics (n=34), antibiotics (n=35), and anti-emetics (n=28).

COST CALCULATION

The average overall cost from a public payer's perspective is €43,782 (95% CI €35,878-€52,441) per patient corresponding to an average cost of €3,919 per month. The hospitalisation cost is the main cost-driving factor with an average of €26,921 per patient, or 61% of the total cost. Chemotherapy administration accounted for 17% (€7,416 per patient) and radiotherapy for 5% (€2,322 per patient). Surgical procedures accounted for 7% (€3,052 per patient). The cost of the oncology visits and day clinic visits from the public payer's perspective accounted for 0.9% (€377 per patient) and 2.5 % (€1104 per patient), respectively. Other cost factors from the public payer's perspective are imaging (2.7 %), drug use (2.4%) and lab tests (2.4%). The average cost from the patient's perspective is €1,383 (95% CI €1,175-€1,603) per patient, corresponding to an average cost of €124 per month. The main cost-driving factor for the patients is also the hospitalisation cost, accounting for 68% of the cost (€946 per patient). The cost of the oncology visits and day clinic visits accounted for 7% (€98 per patient) and 1.4% (€19 per patient), respectively. Imaging tests accounted for 4% (€59 per patient) and medication for 15.5% (€214 per patient).

The group surgery alone has a lower cost than average per patient, €33,736 (95% CI €25,356-€42,913), of which €32,723 was reimbursed by NIHDI. However, due to their low survival time, the average monthly cost for these patients is higher (€11,125). The management costs in patients treated with the Stupp regimen were €58,429 (95% CI €44,719-€73,564), of which €56,758 was reimbursed by NIHDI. The average cost per month was €5,104. The remaining eleven patients who received a different treatment regime had an overall cost of €32,847 (€22,800-€44,048), of which €31,556 was reimbursed by NIHDI.

DISCUSSION

The results of this study were obtained from a real-world setting. Almost a third of the patients (31%) were deemed unsuitable for any adjuvant therapy after biopsy or surgery due to factors as patients' choice, poor general condition, surgical complications or rapidly progressing disease. These patients have a dismal prognosis with a mean OS of 1.6 months. The current standard treatment for newly diagnosed GBM is surgery followed by irradiation with concomitant and adjuvant temozolomide. However, in this real-life setting, only 24 patients (47%) started the standard Stupp regimen. Wasserfallen *et al.* calculated the treatment cost of glioblastoma patients from diagnosis to death from a hospital perspective in a Swiss university hospital in 2003.[4] Patients received biopsy or surgical resection and adjuvant concomitant chemoradiation with temozolomide followed by temozolomide monotherapy. The average (standard deviation [SD]) cost per patient was €39,092 (€21,948), with

KEY MESSAGES FOR CLINICAL PRACTICE

1. In real life, a significant fraction of glioblastoma patients is deemed unsuitable for adjuvant therapy after surgery/biopsy.
2. Overall, the average cost per glioblastoma patient was approximately €45,000.
3. Hospitalisation is the major cost driving factor in treatment and follow-up of glioblastoma patients.
4. The cost for the patients is considerable (€1,400).

a mean (SD) survival time of 22 months (18.4 months). The biopsy group had an average (SD) cost per patient of €30,655 (€19,983), with a mean (SD) survival time of 8.3 months (6.3 months). The surgical resection group had an average (SD) cost per patient of €41,744 (€22,133), with a mean (SD) survival time of 26.3 months (18.8 months). A French study showed an increase in cost of glioblastoma management over time.[5] Three cohorts of newly diagnosed patients were studied from diagnosis to death from a French sickness fund perspective in 2004 before, and in 2008 and 2011 after the widespread introduction of the Stupp regimen. The mean (range) cost of glioblastoma management was €53,368 (€11,181 - €166,145); €70,201 (€20,957 - €182,038) and €78,355 (€26,037 - €273,003) per patient, respectively. Median survival was respectively 10 months; 17 months and 17.5 months. The costs of glioblastoma treatment in the United States are substantially higher than in Europe. Ray *et al.* calculated the total healthcare expenditure in the first twelve months after the initial surgery for glioblastoma.[6] The average (SD) cost in patients managed with radiotherapy and temozolomide was $184,107 ($112,929), with a median survival of 14.2 months. Jiang *et al.* calculated a mean (95% CI) cost of $201,749 ($197,490-$206,024) in a similar patient group; median (interquartile range) follow-up was 14 months (8-24 months).[7] Burton *et al.* calculated the post-surgery treatment cost of elderly glioblastoma patients in the United States.[8] The median (range) cost of management with radiotherapy and temozolomide was $78,784 ($16,644-$452,143) per patient, with a median (range) survival of 11 months (2-56 months). The costs were lower in older studies. Between 1985 and 1992, the mean (range) cost of management of glioblastoma with surgical resection followed by radiotherapy was $25,618 (€16,846-€33,902) per patient in Norway; median (95% CI) survival was 16 months (14-16 months).[9] Between 1996 and 1998, the cost of glioblastoma management was CA$22,447 (€4,679-€36,342) per patient in Canada; mean (range) survival 6.8 months (0.1-27.3 months).[10]

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