

Treatment Costs for Glioblastoma Multiforme in Nova Scotia

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ABSTRACT: Background: Glioblastoma Multiforme (GBM) is the most common and malignant brain tumor in adults. The median survival in patients harboring this neoplasm is 12 months irrespective of any form of therapy. Health care costs of illnesses with high mortality rates, such as GBM, are of particular interest in times of constrained health care resources. No information regarding costs for the treatment of patients with GBM is available in Canada. The aim of this study was to conduct an analysis of the costs of treatment of GBM in Nova Scotia. **Methods:** Patients with histologically proven GBM during a three year period (1996-1998) in Nova Scotia were included in the study. Analysis was based on hospital costs supplemented by data on additional medical services received following discharge for the primary intervention. **Results:** The mean cost of medical care per patient from the time of diagnosis to death was \$ 17,149. The highest costs were related to hospitalization with ward costs alone accounting for 48% of all costs. Radiotherapy costs were 25%, surgery costs were 16% and chemotherapy costs were 7% of all costs. Costs for diagnostic procedures were 6% of the total costs. **Conclusion:** Our data reflect the costs and practice pattern in the treatment of GBM in Nova Scotia and may be of value as an initial attempt to analyze costs of treatment of GBM in Canada.

RÉSUMÉ: Les coûts du traitement du glioblastome multiforme en Nouvelle-Écosse. Introduction: Le glioblastome multiforme (GBM) est la tumeur cérébrale la plus fréquente et la plus maligne chez les adultes. La survie médiane chez les patients porteurs de cette tumeur est de 12 mois, quel que soit le mode de traitement. Les coûts du traitement de maladies ayant un taux élevé de mortalité comme le GBM ont un intérêt particulier en période de contraintes budgétaires dans le domaine de la santé. Il n'existe pas d'information sur les coûts du traitement des patients atteints de GBM au Canada. Le but de cette étude était d'effectuer une analyse des coûts du traitement du GBM en Nouvelle-Écosse. **Méthodes:** Les patients ayant un GBM prouvé par anatomopathologie pendant une période de trois ans (1996-1998) en Nouvelle-Écosse sont inclus dans l'étude. L'analyse était basée sur les coûts hospitaliers et les coûts extrahospitaliers à la suite de l'intervention initiale. **Résultats:** Le coût moyen des soins médicaux par patient à partir du moment du diagnostic jusqu'au décès était de \$17,149. Les frais les plus élevés étaient attribuables à l'hospitalisation, les frais d'hébergement étant responsables de 48% de tous les coûts. Les coûts de la radiothérapie constituaient 25% du total, la chirurgie 16% et la chimiothérapie 7%. Les coûts liés à la démarche diagnostique étaient de 6% du total. **Conclusion:** Nos données reflètent les coûts et le profil de pratique concernant le traitement du GBM en Nouvelle-Écosse et pourraient être utiles comme étape initiale d'une analyse des coûts de traitement du GBM au Canada.

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Glioblastoma multiforme (GBM) is the most common primary brain tumor in adults and accounts for about 2.5% of all cancer deaths.¹ Although approximately 2300 individuals per year develop a brain tumor in Canada,² the incidence of GBM in the country is not known. A recent study in Nova Scotia reported an incidence of GBM of 2.1/100,000 per year.³ The standard treatment for a GBM is neurosurgery (resection or biopsy) followed by radiotherapy and, in some cases, systemic chemotherapy. However, GBM is a highly aggressive neoplasm and the median survival in individuals harboring this tumor is 12 months irrespective of any form of therapy.⁴ Novel therapies such as immunotherapy, gene therapy, the use of antiangiogenesis

compounds and local chemotherapy using implantable biodegradable polymers (Gliadel) are currently being developed. The cost of these types of therapies could be substantial but there

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is little information in the literature regarding the cost of treatment of patients with GBM with standard therapy. Such information would be important in assessing the cost effectiveness of treating a patient with GBM with alternative therapies as they become available.

Although some studies are available regarding the costs for treatment of brain tumors,⁵⁻¹⁰ few studies have analyzed the costs for high grade gliomas.^{5,8,9} No information regarding cost for the care of patients diagnosed with GBM is available in Canada and the results of the foreign studies are not directly applicable as clinical practice patterns and the health care system in Canada are distinctively different. As financial resources within our health care system continue to be strained, the assessment of costs for the care of our patients is crucial. The purpose of this study was to conduct an analysis of the costs of standard treatment therapies for histologically proven GBM from the time of diagnosis until death at the QEII Health Sciences Centre in Halifax, which is the only neurosurgical center in the province of Nova Scotia. Our analysis is based on the in-hospital costs supplemented by data on additional medical services received following discharge for the primary intervention. Our data reflect actual practice rather than protocol-driven care. Furthermore, it provides a picture of care for an entire provincial population, since virtually all Nova Scotia residents with GBM are treated in the Halifax neurosurgical service.

PATIENT COHORT AND METHODS

The inclusion criteria in our analysis was histologically proven GBM. All patients with brain tumors in the province of Nova Scotia are referred to the Queen Elizabeth II Health Sciences Centre for histological diagnosis. At the time of this analysis, standard practice for the treatment of GBM included surgery (craniotomy for resection or stereotactic biopsy), radiation therapy and, in some cases, chemotherapy. All visits to the Cancer Center for radiation therapy and chemotherapy were included in the cost calculations. Although carmustine (BCNU) was used as the main chemotherapeutic agent, costs for different agents or combination of drugs were also included in the analysis. All Nova Scotia residents with proven GBM who were diagnosed in 1996, 1997, and 1998 were included in our study. Data on patient characteristics and treatment at the Queen Elizabeth II Health Sciences Centre was collected retrospectively from patient charts. Data on additional hospitalizations, patient visits to emergency rooms and doctors offices outside the hospital were also collected from provider contact. We organized the utilization data into specific resource categories (Appendix A).

We developed unit costs for each service based on data from local sources. These sources are outlined in Appendix A. Using patient-specific utilization and unit cost data, we derived a cost for each patient for each of the service categories. The costs are presented in the form of descriptive statistics. We report on central tendencies (mean, median and standard deviation), as well as on indicators of high cost outliers.

RESULTS

Patients

A total of 61 patients met the inclusion criteria of the study.

Histological confirmation of a GBM was available for all patients. The demographic characteristics of this group of patients is presented in Table 1. The average patient age was 64 years with a range of 39-90 years. There were 39 males (64%) and 22 females (36%). The average time from diagnosis to death was 206 days with a standard deviation of 189 days. The minimum time of survival from diagnosis was two days and the maximum was 831 days. The distribution of survival times is shown in Table 2.

Costs

The mean cost of medical care per patient from the time of diagnosis to death was \$17,149 with a range of \$4,679 to \$36,342. The breakdown of costs per patient is shown in Table 3. The highest costs were related to hospitalization with ward costs alone accounting for 48% of all costs. The costs for surgical intervention (craniotomy for resection or stereotactic biopsy) accounted for 16% of all mean costs (Table 3). Total hospital costs for patients undergoing craniotomy for resection were \$20,559 versus \$14,782 for patients in whom a stereotactic biopsy was performed (Table 4). The higher costs for craniotomy were related to a longer stay in hospital (a mean of 14 days for craniotomy versus a mean of nine days for stereotactic biopsy) and higher costs of supplies related to the procedure (Appendix A). Cost for diagnostic procedures (radiology and laboratory tests) were very modest and accounted for only 6% of total costs.

Radiotherapy costs accounted for 25% of all costs (Table 3) while chemotherapy costs (medical oncologists and chemotherapy drugs) were 7% of all costs. Patients that received surgery alone, either a craniotomy for resection (n=5) or a stereotactic biopsy (n=13), had mean costs of \$11,921. Patients receiving postoperative radiation had a mean cost of \$18,241 while patients receiving postoperative radiation and chemotherapy had higher costs with a mean of \$22,447 (Table 5).

The mean costs for survival time are shown in Table 6. The mean cost per survival day for patients that survived up to 179 days was \$79. For patients that survived up to 359 days the cost was \$49 per day and for patients that survived up to 720 days, the daily cost was \$34.

DISCUSSION

This study has analyzed the direct costs of treating patients with a proven histological diagnosis of GBM during a three year period in the province of Nova Scotia. Cost analysis of treatment of specific clinical entities is important as constraints in health expenditure continue to increase. Health care costs of illnesses with high mortality rates, such as GBM, are of particular interest in times of constrained health care resources.^{11,12} In the present study 80% of the patients died within one year of diagnosis. We have found that the mean cost of treatment of patients diagnosed with GBM in the province of Nova Scotia is \$17,149 (range \$4,679 to \$36,342). The indirect costs related to the patient's loss of income and the economic impact on their families and community are difficult to determine and have not been analyzed. A United States study suggests that the indirect costs for cancer in the central nervous system are approximately 6.5 times the direct costs.¹³

When the survival time is considered, the daily costs of

Table 1: Characteristics of Patients and Treatments (N=61)

Variable	Frequency/Value
Mean age - years	64.3
Range - years	39 - 90
Sex	
Male	39 (64%)
Female	22 (36%)

Table 2: Survival Times

Mean survival days	206
(Standard deviation)	189
Survival Categories	Number of Patients
1 day to 90 days	21
91 days to 180 days	11
181 days to 270 days	11
271 days to 360 days	6
361 days to 720 days	11
More than 720 days	1

Table 3: Summary of Cost Per Patient

Resource item	Number of Patients	Mean value of costs (standard deviation)	Range
Laboratory tests	61	\$68 (37)	\$32- \$229
Radiation oncology (facility costs and physician fees- received radiation)	43	\$4,263 (1,828)	\$904 - \$6,850
Surgery (room costs, surgeon and anesthesiologist fees and anesthesia drugs)	61	\$2,800 (1,326)	\$1,699 - \$8,178
Diagnostic radiology (inpatient and outpatient)	61	\$977 (634)	\$108 - \$3,461
Inpatient hospitalization - ward costs	61	\$8,179 (6,258)	\$264 - \$25,872
Outpatient pharmaceuticals (only related to treatment)*	54	\$43 (16)	\$11 - \$69
Medical oncologist fees	40	\$229 (167)	\$105 - \$681
Intensive care	31	\$3,090 (3,705)	\$53 - \$14,124
Emergency room (facility and physician)	23	\$120 (85)	\$64- \$321
Chemotherapy-drugs	11	\$951 (801)	\$30-\$2,194
Home care	5	\$3,184 (1,696)	\$1,140- \$5,354
Total of all services	61	\$17,149 (8,092)	\$4,679 - \$36,342

*Only includes decadron, sulcrate and dilantin

Table 4: Total Cost by Procedure

Number of cases	Procedure	Mean	Standard Deviation
25	Craniotomy	\$20,559	\$8,224
36	Biopsy	\$14,782	\$7,195

Table 5: Total Cost of Therapy

Number of cases	Therapy	Mean	Standard Deviation
18	Surgery	\$11,921	\$6,577
32	Surgery + Radiation	\$18,241	\$7,296
11	Surgery + Radiation + Chemotherapy	\$22,447	\$8,451

Table 6: Total Cost by Survival

Number of cases	Days of Survival	Mean	Standard Deviation	Mean cost perday
32	0-179	\$14,204	\$7,282	\$79.00
17	180-359	\$17,701	\$7,171	\$49.00
12	360-720	\$24,221	\$7,260	\$34.00

treatment decreased with longer survival times. A patient surviving up to six months cost \$79 per day while survival prolonged to one year results in costs decreased to \$49 per day. In this study, the majority of patients died within one year of diagnosis and the decrease in costs with survival time reflects the higher costs of initial treatment. The initial treatment period, which included patient hospitalization and surgery, accounted for the majority of costs (64%). This observation has also been made by a recent study looking at cost of care of high-grade astrocytomas.⁵

The costs of surgical intervention were higher if the patient had a craniotomy for tumor resection versus a stereotactic biopsy. This observation is relevant to cost-effectiveness of surgery in GBM in view of the controversy related to the survival benefits of tumor resection versus biopsy.¹⁴ The higher costs for craniotomy are due mainly to increased hospitalization time (14 days versus nine days for stereotactic biopsy) and higher costs of supplies related to the procedure (\$1,144 versus \$64 for a stereotactic biopsy). The costs of anesthesia drugs are included in the calculation of surgical supplies. In our center, stereotactic biopsy is performed using sedation and local anesthesia.

Radiotherapy costs were 25% of the total costs of treatment and 71% of the patients received radiotherapy postoperatively. In this study, radiotherapy appears to be a cost-effective treatment in view of the relatively moderate costs and the available evidence showing that postoperative radiotherapy is more effective in the treatment of GBM than surgery alone.¹⁵⁻¹⁸ The relatively low costs of radiotherapy in our study likely relates to low hospitalization rates. In the majority of cases, radiotherapy is provided as an outpatient service. In contrast, a recent British study looking at the costs of the treatment of malignant glioma at a neuro-oncology clinic showed that the costs of radiotherapy were twice the costs of surgery and neurosurgical beds combined.⁹ These higher costs were associated with in-hospital stays of 14 days for patients receiving radical radiotherapy and seven days for patients receiving palliative radiotherapy.

Only 18% of patients in this study received chemotherapy, accounting for 7% of all costs per patient. The relatively low use of chemotherapy reflects the modest impact of chemotherapy in the treatment of GBM¹⁸ and the practice pattern in Nova Scotia. Canadian studies have reported on the cost-effectiveness of chemotherapy for other types of cancers such as metastatic non-small-cell lung cancer.¹⁹ However, no studies are available regarding costs of chemotherapy for brain tumors in Canada. As new drugs and novel therapies, such as local chemotherapy using implantable biodegradable polymers impregnated with BCNU, for brain tumors become available,^{20,21} analysis of cost-effectiveness of these interventions would need to be compared with the cost of systemic chemotherapy.

In summary, the results of this study reflect the cost and practice pattern in the treatment of GBM in Nova Scotia and may be of value as an initial attempt to analyze the costs of treatment of GBM in Canada, as no information regarding cost for the care of these patients in Canada is currently available.

Future analysis of both the direct and indirect costs of patients with GBM and the impact of resource utilization in quality of life and clinical effectiveness are of paramount importance in determining the cost-effectiveness of neurosurgical intervention for GBM.

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Appendix A: Service categories and unit costs for glioblastoma cases

Type of service	Method of measurement	Cost	Canadian Dollars
Inpatient days	Direct nursing and supplies (including drugs) – costs from a Nova Scotia teaching hospital.	Ward per diem:	264.00
		ICU per diem:	1,284.00
Operating room costs	Direct nursing cost per hour of OR time	Nursing per hour:	22.00
		Other support staff:	
	Craniotomy, per case:	37.00	
	Biopsy, per case	7.50	
	Supplies directly estimated per procedure	Craniotomy:	1,144.00
Laboratory tests	Recovery room costs:1 hour nursing	Biopsy:	64.00
		Recovery:	22.00
Laboratory tests	Total direct costs per workload unit in a Nova Scotia teaching hospital	Venipuncture:	4.31
		routine bloodwork:	28.02
		dilantin level:	14.90
		group and cross match:	11.96
Radiology costs	Include operating costs and physician fees. Total operating costs (support staff, technician costs, supplies, radiology department overhead) allocated to each test according to national workload units. Professional fees are valued according to the provincial schedule of benefits.	CT scan:	
		un-enhanced:	112.22
		enhanced:	118.76
		combined:	157.24
		MRI:	
Inpatient physician fees – surgeon	Provincial schedule of benefits. Craniotomy (code 14.29.c)	non-enhanced:	112.97
		enhanced:	128.42
		Major consult	71.39
		daily visit:	24.84
		craniotomy:	1,118.00
Inpatient physician fees – anesthesiologist	Provincial schedule of benefits; load factor for specific procedures and times.	biopsy:	1,218.00
		post-operative per day:	24.84
		Per hour	130.00
		Per operation (average)	473.00
		Outpatient physician fees	Provincial schedule of benefits.
Emergency room – facility fees	Cost per visit, nursing and ER operating costs	Facility fee per visit	45.00
		Per visit	19.32
Emergency room – physician fees	Provincial schedule of benefits.	Per visit	19.32
Chemotherapy	Cost of drugs to hospital. For drugs taken orally, a publicly set dispensing fee (\$8.85) is added. For intravenously administered drugs, a pharmacy preparation and nursing administration cost of \$22 per hour is added.	Drug cost	
		Pharmacist fee:	8.85
		IV administration (per dose):	22.00
Medical oncology visit	Cost per consult (for those not receiving chemotherapy), and cost per medication administration (for those receiving chemotherapy.) As per provincial billing schedule.	Consult	105.00
		Administration visits	24.25
Outpatient pharmacy costs	Cost of individual drugs from hospital pharmacy. Cost per patient is based on assumed dosing schedule. Pharmacy dispensing fee based on the provincial pharmacist reimbursement rate.	Drug cost	
		Pharmacy fee (per drug dispensed)	8.85
Radiation oncology – facility cost	Facility costs – provincial estimate	Per visit	175.00
		First visit	60.86
		Other visits (per visit)	35.80
Radiation oncology – oncologist visit	Based on provincial schedule of benefits		