ORIGINAL RESEARCH ARTICLE

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Economics of Acromegaly Treatment in Brazil: A Budget Impact Analysis of Pituitary Surgery Compared with Long-Term Octreotide LAR

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Abstract

Background Acromegaly is a rare, chronic and debilitating disease whose treatment places a high burden on health systems. In the reality of the Brazilian public health network, many patients are kept on drug treatment because of barriers to access to surgery.

Objective The aim of this study was to estimate the costs and budget impact of routine transsphenoidal endoscopic surgery in relation to those of long-term drug treatment with octreotide long-acting release (LAR) from a cohort of patients followed at the referral medical centre for acromegaly treatment in the Federal District, Brazil.

Methods Based on micro-costing data collected using mixed methods from a local perspective of the public health system, we performed a budget impact analysis (BIA) on a 3-year time horizon. Uncertainty was handled with deterministic (tornado and scenario) and probabilistic (Monte Carlo simulations) sensitivity analyses.

Results Compared with the continued use of octreotide LAR at a dose of 30 mg every 28 days, the incremental budget impact of conducting two surgeries per month, considering a cure rate of 55%, could bring savings of approximately US$879,362.18 (95% CI 860,176.29–898,548.08) over 3 years. Depending on the key variable values, the savings amplitude ranged from US$431,836.39 to US$1,519,132.04.

Conclusions Improving access to surgery could result in significant cost reductions in acromegaly treatment. The present study stands out for being the first to estimate the costs of transsphenoidal surgery in the context of the public health system in Brazil.

Key Points for Decision Makers

Acromegaly is a rare condition associated with multiple comorbidities and increased mortality.

Medical treatment is usually life-long and entails a high cost.

Improving access to surgery can promote cure and significant cost reductions.

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1 Introduction

Acromegaly is a rare disease with high morbidity and mortality that is complex and expensive to manage [1]. Commonly caused by a pituitary adenoma that overproduces growth hormone (GH) and results in increased levels of

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insulin-like growth factor 1 (IGF-1), acromegaly is associated with chronic complications and impaired quality of life [2, 3]. Despite being a rare disease, its related comorbidities and requirement for life-long management suggest that this disease can place a considerable burden on health systems [1].

The therapeutic approach to acromegaly is multimodal; it can entail surgery, medications and radiotherapy, used alone or in combination. Transsphenoidal surgery is the first line of treatment for most cases because of the considerable chance of complete removal of the tumour when the procedure is performed by an experienced neurosurgeon [2–4]. However, in low- and middle-income countries, surgery may not be feasible due to difficulties related to the structure of the public health system. Medications are indicated for patients with persistent disease following surgery or as a primary treatment; the medications include somatostatin analogues, cabergoline and pegvisomant [4].

In Brazil, for rare diseases, including acromegaly, diagnosis and treatment criteria in the public health system are defined by published Clinical Protocols and Therapeutic Guidelines [5], which provide pharmacological treatment strategies for only the first two medications (somatostatin analogues and cabergoline). Conventional radiotherapy is also available through the public health system, but it is considered an adjuvant treatment and reserved only for selected cases [4].

Studying the costs of healthcare services is essential for efficient resource allocation and healthcare [6–8]. In many cases, this information is obtained via cost-effectiveness analysis, an economic evaluation that comprises an analysis of costs (costing study) and the effects (benefits) of a healthcare intervention [6]. In this field, budget impact analyses (BIA) are an important tool complementary to economic evaluation that are able to estimate the financial consequences of adopting and disseminating a new strategy or technology in a given health system [9]. If properly performed, budget impact studies can predict how the change in the supply of inputs or services will influence the future costing of a health problem [10].

Considering that the costs of treating acromegaly can be high [11, 12], economic studies with the objective of promoting the best possible use of public resources are essential to ensure continuity in the lines of care, especially in times of budget constraints [13]. Although there exists a range of cost studies in Brazil, including real-world data studies with large samples [14, 15], the results of a systematic review on BIA [16] have found that 95% of the papers were published in Europe and the US. In addition, the authors conclude that there was a low adherence to key characteristics of BIA and strong conflict of interest in the published studies. Thus, these economic studies are still scarce in Brazil, potentially affecting policy planning in the public health system [17].

To our knowledge, the budget impact of pituitary surgery compared with that of long-term pharmacological therapy with somatostatin analogues has not been assessed in published studies.

2 Objectives

The aim of this study was to estimate the budget impact of transsphenoidal surgery compared with that of the long-term use of octreotide long-acting release (LAR) (somatostatin analogue currently available through the local public health system) at the main centre for acromegaly treatment in the Federal District, Brazil.

3 Materials and Methods

3.1 Context, Time Horizon and Perspective

The Neuroendocrine Unit of the Brasilia University Hospital, which belongs to the public health system and is a tertiary centre of attention, comprises the main centre for pituitary diseases in the Federal District. The BIA evaluated the affordability of pituitary surgery for acromegalic patients undergoing octreotide LAR use (patients with active disease and need of medication) at the referral medical centre in both Brasilia (Brazil's capital) and the metropolitan region.

A 3-year time horizon was used disregarding conventional economic adjustments (discount rate and inflation) in accordance with recommendations from methodological guidelines for BIA [9, 18]. The calculations were performed using Microsoft Excel® software, adopting the local public health system's payer perspective. Costs were converted to US dollars assuming an exchange rate of 1.00 USD = 3.22 R$ in January 2018.

3.2 Population

The eligible population was estimated in a dynamic fashion, trough measuring the hospital demand and applying the incidence estimates to predict the entrance of new patients. Considering the analysis of a long-term follow-up of a cohort of 111 patients seen at the referral medical centre by 2014 (unpublished data), the total number of patients using somatostatin analogues in the year 2018 was estimated. Patient prediction at the beginning of the model and insertion of new patients were based on the annual onset rate of somatostatin analogue treatment over the last 10 years (2005–2014). We considered that all patients using somatostatin analogues could benefit from surgery, as it is considered the first-line treatment and reoperation should be evaluated when the first surgery is not effective [4].

3.3 Effectiveness of Surgery

The expected cure rate was obtained from a literature review [19–24], which supported estimates for the cure rate of the disease being between 40 and 70% among patients subjected to surgery. Among other factors related to adequate performance of the procedure, this rate can be affected by team experience and technical conditions.

3.4 Costs of Transsphenoidal Surgery

A mixed macro- and micro-costing technique [6, 25–27] was used to estimate the costs of endoscopic transsphenoidal surgery. Through consultation with specialists and other health professionals, the costs of the operating room, medications and materials usually used in the surgery; medical and auxiliary fees; use of special materials; expenses related to equipment maintenance; and daily rates for the intensive care unit (ICU) and general hospital ward were obtained.

A portion of these costs was provided through macro-costing by the Department of Health Costs of the Secretariat of Health of the Federal District, which participates in the National Programme for Cost Management of the Ministry of Health, whose methodology is based on absorption costing [28]. However, because this division was only recently implemented and could not measure specific values by procedure, it was necessary to estimate some cost components by micro-costing. Data regarding special material specific for neurosurgery and medications and general materials used in the operating room were obtained through this method.

To define the special materials for transsphenoidal surgery, three neurosurgeons with experience in conducting this type of procedure were consulted about the items that they considered necessary to carry out the surgery under suitable conditions. The items listed for each one were compared, and those that were noted by the majority were selected for costing (Table S1, see electronic supplementary material).

Drugs and materials used in the operating room were determined with the help of an anaesthesiologist, with the goal of including items that are usually used in this type of procedure. Subsequently, each item was looked up separately in our main price source, the computerized system (Alphalinc®) of the Secretariat of Health for the management of stock data of medications and medical-hospital materials (Table S2, see electronic supplementary material). In addition, the Department of Health Costs made available the charges for the operating room, the average costs related to the maintenance of equipment, and the medical and auxiliary fees based on a 6-h surgery. The current daily rates for the ICU and hospital were also reported.

The depreciation of equipment commonly handled by neurosurgeons and the anaesthesiologist was not calculated by a formal method. However, to minimize this limitation, the equipment maintenance calculation was adopted. This strategy was considered robust given the permanent nature of this type of apparatus.

3.5 Costing of Octreotide LAR

The value for octreotide LAR acquisition was obtained through consultation in Alphalinc®. The presentation of 30 mg was considered because this is the most commonly used dose. Consistent with Brazilian guidelines, the assumption of 12 ampoules was used to estimate the annual cost [6].

3.6 Scenarios

The reference scenario was defined as the situation in which all patients were maintained under medical treatment with octreotide LAR because transsphenoidal surgery was unattainable due to local difficulties in the public health system. Alternative scenarios were delineated with different possibilities for the key parameters according to the surgery coverage: minimal (up to one surgery per month), mean (up to two surgeries per month) and maximum (up to four surgeries per month).

Thus, the base case of this analysis considered the mean coverage of 24 surgeries per year, the mean estimate of surgery effectiveness, surgery costs, and octreotide LAR costs (Table 1).

3.7 Sensitivity Analysis

With the variations of the main estimates included in the model, deterministic (tornado analysis) and probabilistic (Monte Carlo simulations) sensitivity analyses were conducted.

The tornado analysis considered the impacts of the minimum and maximum values of each variable in relation to

Table 1 General evaluation of the different scenarios proposed in the budget impact analysis (BIA)

Parameter	Possible scenarios		
	Base	Minimum	Maximum
Coverage of surgery (surgeries/year)	24	12	48
Effectiveness of surgery (%)[a]	55	40	70
Cost of surgery (US$)[b]	8935.07	7148.06	10,722.08
Cost of annual treatment with octreotide LAR (US$)[b]	19,035.24	15,228.19	22,842.29

LAR long-acting release

[a]Minimum and maximum values obtained from a literature review [19–24]

[b]Minimum and maximum values obtained from the application of ±20% of variation

the base case. Holding the surgery coverage parameter in the base, minimal and maximum values, the probabilistic analysis considered simulations with random selection in a uniform distribution of the range of possible values of the other key parameters (effectiveness and costs).

The variations considered the precision of the data identified in the literature (surgery effectiveness) and specialist opinion (surgery coverage). As an exception, although not being routinely recommended by methodological guidelines [9, 18], for the particular case of the surgery cost and drug prices, where there was no robust variation evidence, a conservative ± 20% amplitude was included (Table 1).

4 Results

In 2014, 54 patients used somatostatin analogues. The rate of onset of new treatments was 5.5 new cases/year considering data in the last 10 years. Applying this rate to the data, the numbers of patients in the years 2018 ($n = 78$), 2019 ($n = 84$) and 2020 ($n = 90$) were estimated.

Table 2 Micro-costing results of transsphenoidal surgery by endoscopic technique in Brasilia, Brazil

Cost specifications	Value (US$)
1. Operating room	160.04
2. Medications and general material used in the operating room	541.01
3. Average cost related to equipment maintenance	38.45
4. Medical fees for surgery	730.91
5. Other professional fees for surgery	111.25
6. Special materials for transsphenoidal surgery	1969.17
7. ICU daily rates (3 days)	3993.39
8. Hospital daily rates (2 days)	1390.85
Total	8935.07

ICU intensive care unit

4.1 Costs of Transsphenoidal Surgery

When considering a transsphenoidal surgery without major intercurrences followed by hospitalization for 3 days in the ICU and 2 days in the hospital, the average cost was estimated at US$8935.07, which included general expenses accumulated up to the patient's discharge (Table 2).

4.2 Annual Cost per Patient for Octreotide LAR

The cost for octreotide LAR 30 mg found in Alphalinc® was US$1586.27, reflecting an annual cost of US$19,035.24. It should be emphasized that this is the somatostatin analogue currently available in the Federal District.
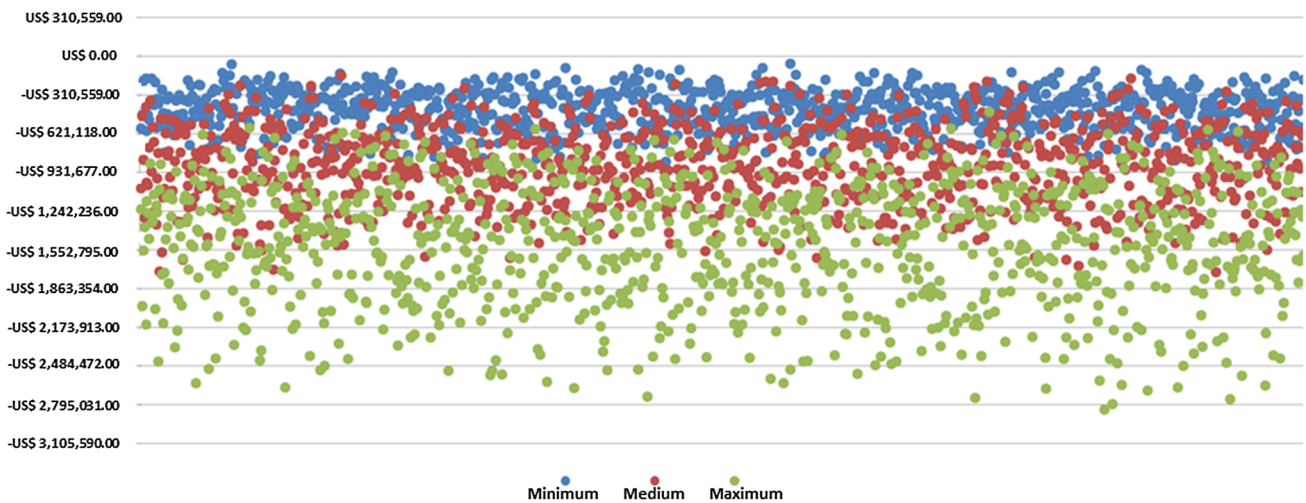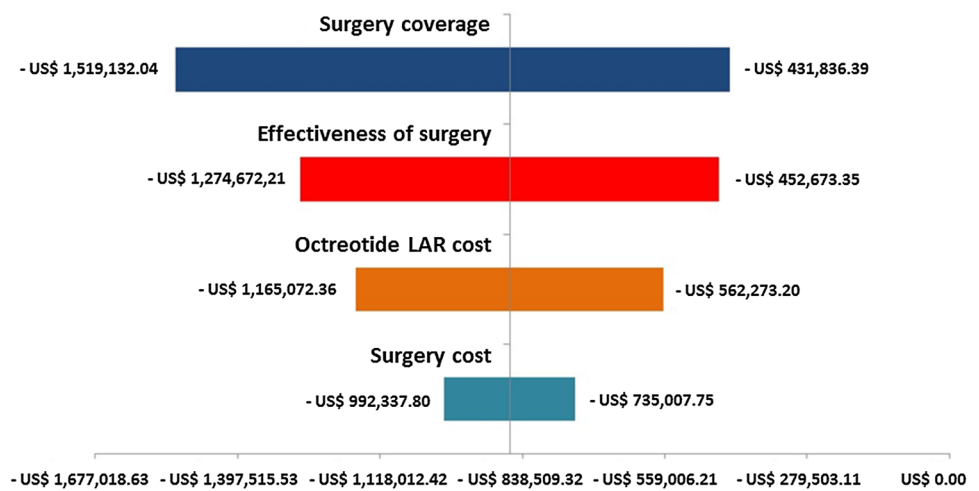
4.3 Budget Impact Analysis (BIA)

The results of the budget impact model were obtained after running the different planned scenarios. In the base case, providing surgery coverage at two procedures per month can bring savings of approximately –US$863,672.78 over 3 years (Table 3).

In comparison, the coverage of one surgery per month and up to four surgeries per month can alter the savings from − US$431,836.39 to − US$1,519,132.04, respectively. These data were robust in the sensitivity analysis, demonstrating a saving of resources in all the proposed scenarios. As noted in the tornado sensitivity analysis, the coverage and effectiveness of surgery are the variables that have the greatest impact on the results (Fig. 1).

In the probabilistic model with 1000 Monte Carlo simulations, the distribution of the budget impact estimates resulted in a mean savings of US$879,362.18 (95% CI 860,176.29–898,548.08) in the average coverage scenario. The budget varied from − US$427,088.49 (95% CI − 417,226.92 to − 436,950.06) to − US$1,509,229.14 (95% CI − 1,479,453.78 to − 1,539,004.51) in the minimum and maximum surgery coverage scenarios, respectively (Fig. 2).

Table 3 Budget impact results of acromegaly treatment with surgery and medication in a 3-year time horizon, Brasilia, Brazil

	2018	2019	2020	Total US$ (2018–2020)
Estimated population	$n = 78$	$n = 84$	$n = 90$	
Reference scenario[a]	US$1,484,164.62	US$1,598,331.13	US$1,712,497.64	US$4,794,993.39
Alternative scenario[b]	US$1,447,440.02	US$1,310,444.20	US$1,173,440.39	US$3,931,320.61
Estimated impact	− US$36,724.60	− US$287,890.93	− US$539,057.25	− US$863,672.78

LAR long-acting release

[a]Reference scenario refers to continued octreotide LAR use and no improvement from surgery

[b]Alternative scenario refers to improvement from transsphenoidal surgery considering two surgeries per month and a cure rate of 55%

Fig. 1 Variation of incremental budget impact according to changes in the assumptions of the model. *LAR* long-acting release

Surgery coverage

- US$ 1,519,132.04   - US$ 431,836.39

Effectiveness of surgery

- US$ 1,274,672,21   - US$ 452,673.35

Octreotide LAR cost

- US$ 1,165,072.36   - US$ 562,273.20

Surgery cost

- US$ 992,337.80   - US$ 735,007.75

- US$ 1,677,018.63   - US$ 1,397,515.53   - US$ 1,118,012.42   - US$ 838,509.32   - US$ 559,006.21   - US$ 279,503.11   US$ 0.00

US$ 310,559.00
US$ 0.00
-US$ 310,559.00
-US$ 621,118.00
-US$ 931,677.00
-US$ 1,242,236.00
-US$ 1,552,795.00
-US$ 1,863,354.00
-US$ 2,173,913.00
-US$ 2,484,472.00
-US$ 2,795,031.00
-US$ 3,105,590.00

Minimum   Medium   Maximum

Fig. 2 Distribution of possible scenarios of budget impact according to the coverage of surgery. Each point reflects the budget impact result of one Monte Carlo iteration according random draws of the pre-defined range of the main factors values

5 Discussion

Potentially enhanced by a long and time-consuming queue for transsphenoidal surgery, a large number of patients are using somatostatin analogues in our setting. Several patients are receiving pharmacotherapy as an initial treatment because of non-availability of the procedure. This situation is not rare, as barriers such as accessibility, availability, affordability and acceptability of surgical care are common in low- and middle-income countries [29]. On the other hand, the estimated high costs of pharmacological therapy, approximately US$19,000.00 per patient per year, also demands a robust social protection system to prevent inequity issues in access to medicines [30]. These results

reinforce the necessity of interventions to improve surgical care coverage.

Along with clinical and quality-of-life benefits for the patient [31], our BIA showed that improving access to surgery would be associated with economic benefits due to a significant reduction in public health system expenses. Savings of over US$400,000.00 could be reached at the end of 3 years, even in the most conservative scenario. Regarding the results generalization to the average target population, even knowing that the results of surgery are better in microadenomas, we decided to adopt a conservative cure rate of 55% (40–70%), avoiding savings overestimation (a potential result with higher cure rates). Optimizing this scenario can result in even greater savings. In the experience of a

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public tertiary reference centre for pituitary neurosurgery in northeast Brazil, reaching a cure rate of 75% was possible with endoscopic transsphenoidal surgery [22]. This statistic demonstrates that the achievement of good surgical results is plausible in similar contexts of the public health system if appropriate actions are implemented, which is consistent with the evidence that even in low- and middle-income countries, interventions to improve surgical care can be cost effective [30, 31].

Moreover, with better surgery coverage, a greater possibility of pharmacological control in cases with no curative perspective can also be expected, which would also result in savings. Even when it is not possible to completely remove a tumour due to anatomical reasons, the resection of all possible tumour tissue (debulking) promotes a better response to drug treatment, which could lead to the use of lower doses of somatostatin analogues and a reduction in costs of treatment [4, 32–34].

Our results are also consistent with the implementation of recent clinical recommendations, as the latest acromegaly guidelines from the Endocrine Society reinforce and prioritize surgery as the treatment of choice for most patients because it can produce immediate lowering of GH levels and provide tumour tissue for pathological characterization [4]. Currently, these recommendations are not implemented in our service due to issues inherent to the public health system in the Federal District, especially a lack of local investment and planning for surgery.

A strength of the present economic study is its accurate reflection of the local reality, both in the estimation of costs and in the estimation of the population. The costs are highly representative, as they were collected via validated methods in macro- and micro-costing, including absorption costing, database registries and interviews. Our clinical setting is based on data obtained via the historical analysis of a 10-year service follow-up. Considering the current population of the Federal District, approximately 3,000,000, the rate of treatment initiation assessed as six new cases per year is not overestimated relative to the disease incidence rate, usually documented in approximately three to four cases per million [35] and is consistent with barriers to diagnosis and access to medical care.

This study conducted all analyses according to the latest guidelines of the Ministry of Health of Brazil [18], which follows the International Society for Pharmacoeconomics and Outcomes Research (ISPOR) recommendations [9]. The results were robust through both deterministic and probabilistic sensitivity analyses with Monte Carlo simulations. The tornado diagram showed that coverage of surgery and its effectiveness are the parameters that have the greatest repercussions on the magnitude of the reduction of costs.

However, the study also has limitations that should be taken into account when the results are interpreted. It is important to mention that the estimated cost of surgery was performed from the perspective of a single centre in Brasilia. Even though it is feasible to extrapolate the results to the entire Federal District, it is important to consider the main differences in healthcare management when applying the results to other settings in Brazil.

Another limitation is the fact that costs related to complications of surgery, adverse effects of drug treatment and complications of acromegaly in inadequately treated patients were not evaluated. Although transsphenoidal surgery is considered a safe procedure with a low incidence of delayed complications [36], some immediate complications can occur. Nevertheless, the incidence of these complications is considered very low, not invalidating our model. In a series of more than 1100 surgeries, endocrine complications, including transient diabetes insipidus (4.3%), symptomatic hyponatraemia (4.2%) and new hypopituitarism (any axis, 3.6%), were the most frequent. Serious events, such as mortality (0.1%), occurred in < 3% of patients [37]. In relation to drug therapy, there are potential side effects of long-term use. According to published follow-up data, approximately 25% of patients can develop gallstones, usually during the first year of treatment [38]. Cholelithiasis is a risk of somatostatin analogue therapy, but most patients with cholelithiasis are asymptomatic and rarely develop cholecystitis [38]. Thus, despite some limitations, the conclusions of our model are still robust considering that drug side effects would probably enhance the savings observed.

It is also important to reinforce that the BIA is a complementary study to an economic evaluation. For a complete body of evidence, results from an economic evaluation that considers not only the monetary benefits but also the consequences on health, such as cost-effective and cost-utility analyses, are highly recommended [6]. Yet, with all the adopted scenarios supporting decisions in favour of surgery due to resource savings, we believe that our results already provide convincing evidence for improving access to surgery for patients with acromegaly treated in the public health system. As one of the main implications for practice, supported by our results, we hope that the surgery access could be a priority issue to be discussed in future acromegaly guidelines revisions by the Ministry of Health.

6 Conclusions

The BIA showed that significant savings could be achieved by improving access to transsphenoidal surgery. This research within the Federal District has generated important public information that can be applied to the local planning of actions with the objective of improving the quality of care for acromegalic patients and reducing the costs associated with treatment.

Compliance with Ethical Standards

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