www.jmscr.igmpublication.org
Index Copernicus Value: 79.54
ISSN (e)-2347-176x ISSN (p) 2455-0450
crossrefDOI: https://dx.doi.org/10.18535/jmscr/v7i2.99

IGM Publication
Journal Of Medical Science And Clinical Research
An Official Publication Of IGM Publication

Original Article

Factors Predicting Outcome of Acromegalic Patients Undergoing Pituitary Surgery

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Abstract

Introduction: *Acromegaly is a chronic, insidious, debilitating disease, which occurs due to chromophobe adenoma of the pituitary resulting in excessive secretion of growth hormone in an adult. Anaesthetic implication of this disorder is particularly important in terms of changes in the upper airway and increased chances of pulmonary and cardiovascular complications.*

Aim: *The aim of our study was to determine factors predicting the outcome of acromegalic patients undergoing pituitary surgery in terms of duration of intensive care unit (ICU) and hospital stay.*

Methods: *For this retrospective study, data were collected from the records of all patients undergoing pituitary surgery for acromegaly during the period from January 2005 to December 2012 at AIIMS New Delhi. Demographics, type of surgery, size of the pituitary tumor, preoperative investigations and intraoperative data like blood loss, duration of anaesthesia and surgery and perioperative complications were noted. Data were also collected for postoperative recovery profile, duration of mechanical ventilation, intensive care unit and hospital stay. The Glasgow coma scale and outcome scale at discharge were recorded.*

Statistical Analysis: *Data are presented as Mean (SD), Median (Range) or number (%). Continuous variables were analysed using Wilcoxon rank-sum test whereas categorical variables were subjected to Pearson's Chi square tests. Statistical dependence between two variables was calculated using Spearman's rank correlation test.*

Results: *One hundred and twenty-nine patients that were operated for pituitary tumours causing acromegaly during the study period were included. The size of tumour, intraoperative blood loss, intraoperative complications, duration of surgery and anaesthesia, total fentanyl consumption and duration of postoperative mechanical ventilation affected the ICU stay whereas the duration of symptoms, size of the tumour, duration of surgery and anaesthesia and the duration of postoperative mechanical ventilation affected the total hospital stay. There was mortality in 3 patients (2.3 %) while 7 patients (5.4 %) had moderate disability (diminution of vision) at discharge while 119 (92.2 %) patients showed good recovery. Postoperative complications were significantly associated with prolonged ICU stay and hospital stay. ($p = 0.001$ and 0.002, respectively).*

Introduction

Acromegaly is a chronic, insidious, debilitating condition, which occurs due to chromophobe adenoma of the pituitary resulting in excessive secretion of growth hormone in an adult[1]. These patients often have multi system involvement including respiratory, neurological, neuromuscular and skeletal systems. Anaesthetic implication of this disorder is particularly significant in terms of changes in the upper airway and increased chances of pulmonary and cardiovascular complications[2].

Acromegaly was first described by Pierre Marie in 1886. It is seen in both men and women of middle age group. It has an estimated prevalence of 50-60 cases per million and an incidence of 3 to 4 cases per million per year[3]. It is characterized by thickening of the subcutaneous tissues of the scalp, lips, tongue, face, hands, feet, overgrowth of the frontal sinuses, jaw and distal phalanges. The soft tissue and bony changes develop slowly over decades. There is also overgrowth of hair and sebaceous glands. The patients are asthenic which causes slackening of ligaments with kyphosis, scoliosis and sometimes lordosis, so that the enlarged hands hang below the knees. There is atavistic appearance of an individual with acromegaly produced by the beetling brows, prognathous jaw, and overgrowth of hair on the chest[4].

The acromegalic involvement of the upper airway is the most important concern for the anaesthesiologist. It occurs due to overgrowth of the upper airway, increased length of the mandible, epiglottis and cords[5]. Sleep apnea, which can be central, obstructive or mixed due to polypoid masses in the pharynx can be present in these patients. In addition, laryngeal stenosis and cricoid narrowing may also be present. The basal metabolic rate is high. Most individuals have neurological and musculoskeletal symptoms, including headache, nerve entrapment and paraesthesia (often due to carpal tunnel syndrome), muscle weakness and arthralgia. The cartilage hypertrophy and osseous overgrowth often leads to degenerative arthritis, or even spinal stenosis[6]. Once it is suspected, ideally, advance tests like basal or random growth hormone (GH) assay are employed to confirm the diagnosis. The concentration of GH is measured and failure of hormone concentration to decrease 1-2 hours after the ingestion of 75-100g of glucose is presumptive evidence of acromegaly. A radiograph of the skull and CT scan shows enlargement of sella turcica.

Management of anaesthesia for these patients is of prime concern with proper safety and appropriateness. Systemic involvement should always be kept in mind while administering anaesthesia to these patients. Hypertension occurs in 1/3 cases, half of which have increased left ventricular mass or left ventricular wall thickness. Though, it is not well proven, whether cardiomyopathy occurs, acromegalics may develop congestive cardiac failure in the absence of another known underlying heart disease[7]. The incidence and severity of cardiac hypertrophy relates to the duration of the disease, but there are no data to support a relationship between the degree of cardiac enlargement and GH concentrations[8]. When lung function is assessed in patients with an absence of associated cardiac complications, studies confirm that gas exchange in acromegalic patients is normal. Pulmonary function tests are consistent with extrathoracic obstruction as the cause of pulmonary complications. Flow-volume loops reveal greater impairment of expiration than inspiration[9]. The acral enlargement consistently involves upper airway redundancy which includes pharyngeal and tracheal changes that can also lead to airway complications. Over secretion of GH with acromegaly produces resistance to the effects of insulin, which leads to glucose intolerance. This finding remains important as hyperglycaemia is known to worsen cerebral ischaemia[10].

Aim of the Study

- The aim of our study is to determine factors predicting the outcome of acromegaly patients undergoing pituitary surgery.

- The main outcome was in terms of duration of intensive care unit (ICU) and hospital stay after pituitary surgery in acromegaly patients.

Methodology

After approval from the local ethics committee for this retrospective study, data was collected from the records of all acromegalic patients undergoing pituitary surgery during the period from January 2005 to December 2012 at AIIMS, New Delhi. Demographics, size of the pituitary tumor, preoperative investigations and intraoperative data like blood loss, duration of anaesthesia and surgery, type of surgery and perioperative complications were noted. Data were also collected for postoperative recovery, duration of mechanical ventilation, duration of intensive care unit (ICU) and hospital stay. The Glasgow coma scale and outcome scale at discharge were also noted.

Statistical Analysis

Data are presented as Mean (SD), Median (Range) or number (%). Continuous variables were analysed using Wilcoxon rank-sum test whereas categorical variables were subjected to Pearson's Chi square tests. Statistical dependence between two variables was calculated using Spearman's rank correlation test. The value of $P < 0.05$ was considered significant.

Results

One hundred and twenty-nine acromegaly patients were operated for pituitary tumours during the study period. Sixty one females (47 %) and 68 males (53%) with an age of 35.7 (9.5) years and weight of 72.2 (15.5) kg were assessed. The patient demographics and perioperative data is shown in Tables 1 and 2.

Airway related findings are shown in Table 3. The intraoperative and postoperative complications are listed in Table 4 and recovery characteristics are detailed in Table 5.

There was mortality in 3 patients (2.3 %) while 7 patients (5.4 %) had moderate disability (diminution of vision) at discharge while 119 (92.2 %) patients showed good recovery (Figure 5)

The size of tumour ($\rho = 0.19$), intraoperative blood loss ($\rho = 0.5$), intraoperative complications ($\rho = 0.26$), duration of surgery and anaesthesia ($\rho = 0.36$ and 0.33 respectively), total fentanyl consumption ($\rho = 0.22$) and duration of postoperative mechanical ventilation($\rho = 0.50$) affected the ICU stay while duration of symptoms ($\rho = 0.20$), size of the tumour ($\rho = 0.22$), duration of surgery and anaesthesia ($\rho = 0.23$ and 0.24 respectively), postoperative mechanical ventilation ($\rho = 0.31$) and ICU stay affected the total hospital stay. Postoperative complications were significantly associated with prolonged ICU stay and hospital stay. ($p = 0.001$ and 0.002, respectively)

Table 1: Demographic and perioperative data expressed as mean (SD) or N (%).

S.No.	Variables (n = 129)	Mean (SD) or N (%)
1.	Age (yrs)	35.7 (9.5)
2.	Sex Males Females	68 (53 %) 61 (47 %)
3.	Weight (kg)	72.3 (15.6)
4.	Duration of symptoms (yrs)	4.2 (3.5)
5.	Comorbidities Hypertension Diabetes mellitus Both Hypothyroid None	19 (14.7 %) 19 (14.7%) 13 (10 %) 10 (7.7 %) 68 (52.7 %)
6.	Type of Surgery TNTS SLTS Endoscopic TNTS Craniotomy	 45 (34.9 %) 65 (50.3 %) 11 (8.5 %) 8 (6.3 %)
7.	Preoperative Haemoglobin (g %)	12.2 (1.5)
8.	Size of the tumour (sq cm)	8.8 (7.8)

TNTS – Trans-nasal trans sphenoidal surgery
SLTS – Sub labial trans sphenoidal surgery

Table 2: Demographic and perioperative data expressed as mean (SD) or N (%).

1.	Type of Maintenance anaesthesia	Inhalational TIVA	114 (88.4 %) 15 (11.6 %)
2.	Amount of crystalloids infused (ml)		1835.6 (662.6)
3.	Blood Loss (ml)		277.6 (254.8)
4.	Duration of surgery (min)		128.5 (67.0)
5.	Duration of anaesthesia (min)		188.6 (78.0)
6.	Total opioid consumption (µg)		251.5 (65.5)

TIVA – Total intravenous anaesthesia

Table 3: Airway in Acromegaly patients expressed as N (%)

S. No.	Airway		N (%)
1.	DIFFICULT MASK VENTILATION	Yes	13 (10.1 %)
		No	116 (89.9 %)
2.	INTUBATION	Easy	102 (79 %)
		Difficult	27 (21 %)
3.	DEVICE USED	DL	103 (79.8%)
		CMAC	8 (6.2 %)
		Bougie assisted DL	14 (10.8 %)
		Fibreoptic	4 (3.2%)
4.	CL GRADE	I	59 (45.7%)
		II	42 (32.6 %)
		III	21 (16.3 %)
		IV	7 (5.4 %)
5.	ATTEMPTS	1st	113 (87.7 %)
		2nd	13 (10 %)
		3rd	3 (2.3 %)

DL – Direct Laryngoscopy
CMAC – Videolaryngoscope
CL grade – Cornack Lehane Grading

Table 4: Intraoperative and postoperative complications expressed as N (%)

S.No.	Variables		N (%)
1.	INTRAOPERATIVE COMPLICATIONS	None	113 (87.6 %)
		Bradycardia/Hypotension	2 (1.6 %)
		Tachycardia/Hypertension	6 (4.7 %)
		Desaturation	1 (0.8 %)
		Massive Blood Loss	3 (2.3 %)
		Arrhythmias	2 (1.6 %)
		Reexploration	2 (1.6 %)
2.	POSTOPERATIVE COMPLICATIONS	None	66 (51.2 %)
		CSF Leak	32 (24.8 %)
		Electrolyte imbalance	14 (10.9 %)
		Hydrocephalus	2 (1.6 %)
		Pneumonia	7 (5.4 %)
		Rexploration	5 (3.9 %)
		Epistaxis	3 (2.3 %)

Table 5: Duration of Ventilation, ICU stay and hospital stay expressed as Median (Range)

S.No.	Variables	Median (Range)
1.	Preoperative GH levels (ng/ml)	40 (0.05-1260)
2.	Duration of Ventilation (hours)	0 (0 – 240)
3.	ICU Stay (days)	1 (1-10)
4.	Hospital Stay (days)	12 (4-34)

GH – Growth hormone

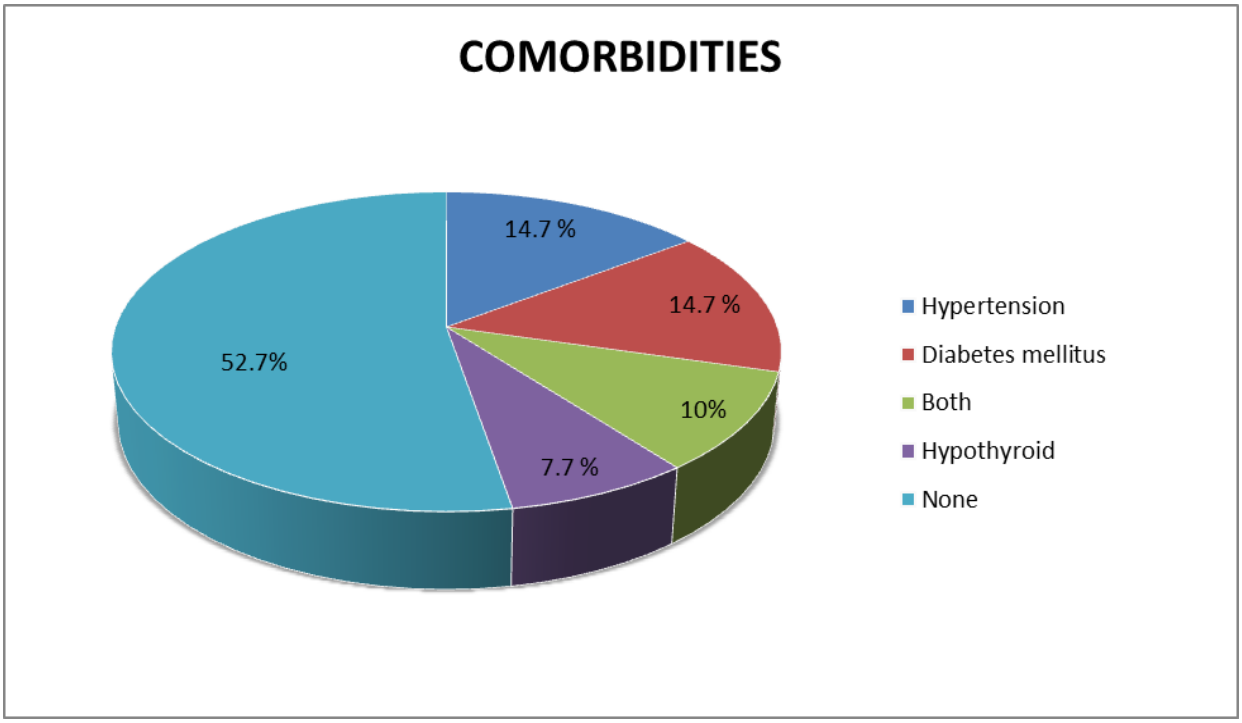

Figure 1 : Comorbidities [N (%)]

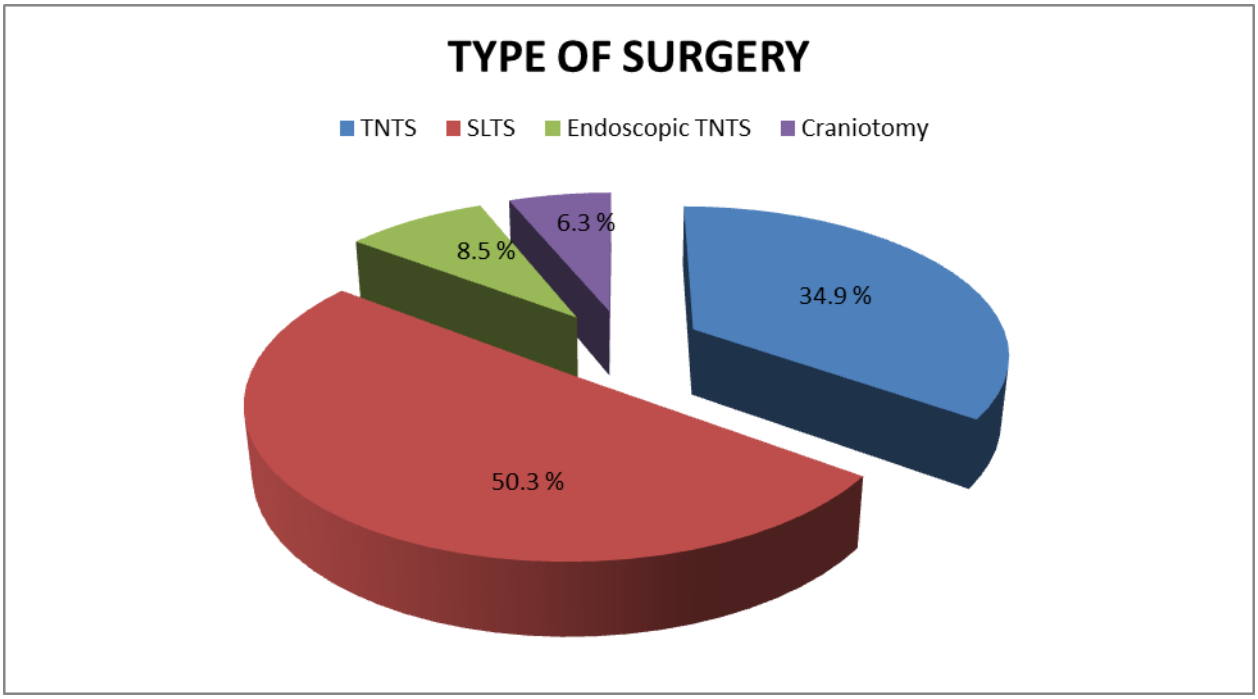

Figure 2: Type of surgery [N (%)]

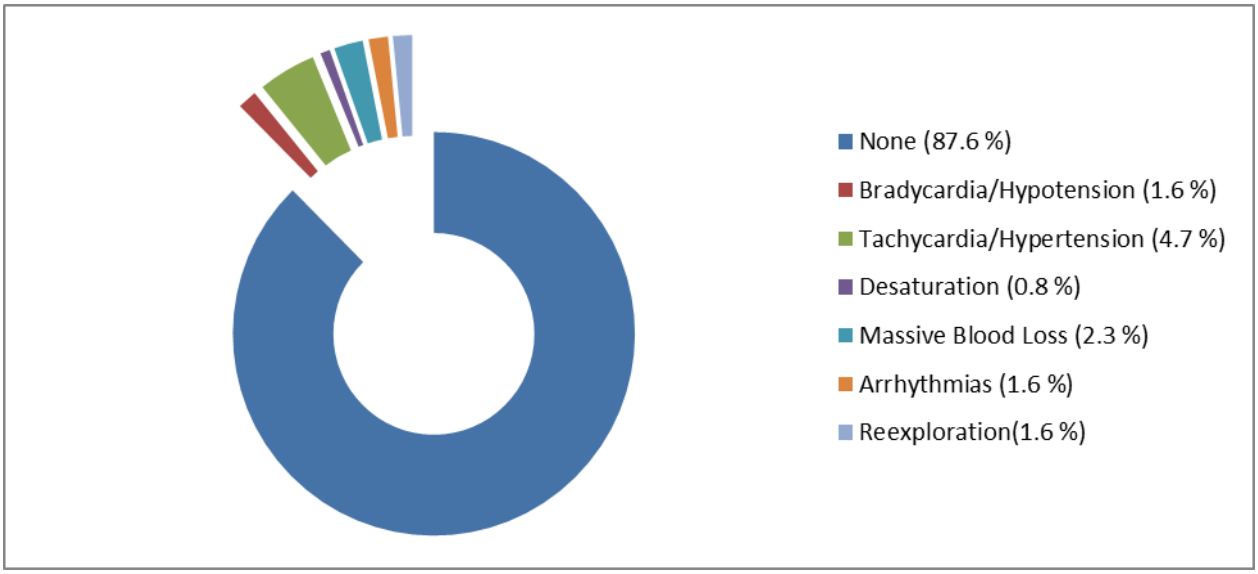

Figure 3: Intraoperative complications [N(%)]

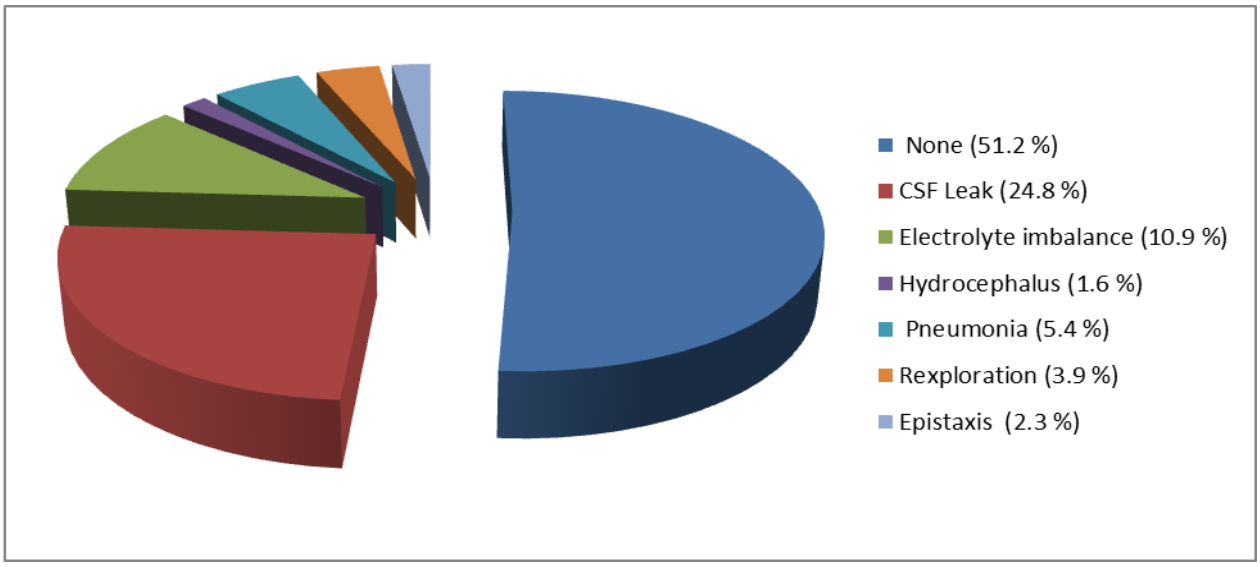

Figure 4: Postoperative complications [N(%)]

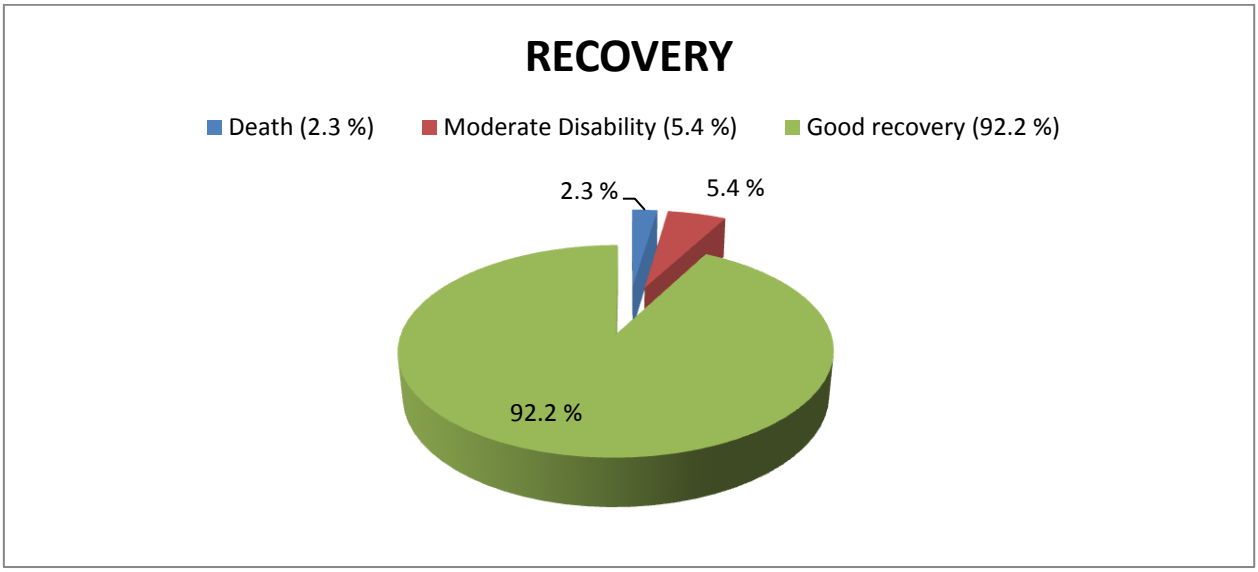

Figure 5: Recovery characteristics [N(%)]

Discussion

The anaesthetic risks of acromegaly include difficulties in airway management, hypertension, and cardiac, gastrointestinal and renal problems. To estimate the incidence of major complications in acromegaly patients, Seidman et al[11] reviewed 28 patients with this condition who had pituitary tumour excision over a 10-yr period. Each patient was matched for age, weight and sex to a non-acromegalic patient undergoing transsphenoidal pituitary surgery. Acromegalic patients received significantly more fentanyl and midazolam and less thiopental and succinylcholine than controls ($P < 0.05$). Mean arterial pressure (baseline, minimal and maximal values) was higher in acromegalic patients than in controls. There was no difference between groups in the use of vasoactive drugs. The partial pressures of oxygen and carbon-dioxide and fraction of inspired oxygen were similar in both groups. Arterial pH was significantly lower ($P = 0.015$), blood glucose was higher ($P < 0.001$) and fluid intake minus output was higher ($P = 0.04$) in acromegalic patients than in controls. Airway difficulty and tongue enlargement were encountered more often in acromegalic patients ($P = 0.002$ and $P = 0.001$, respectively). Their data confirms that in acromegalic patients: airway difficulties occurred more frequently; severe haemodynamic instability did not typically occur during surgery for acromegaly; pulmonary gas exchange was not altered during operation; glucose intolerance was an intraoperative problem; and fluid regulation had to be altered accordingly.

Gittoes et al[12] studied the outcome of pituitary surgery for acromegaly and concluded that surgical outcome for acromegaly is enhanced if patients are operated on by a single experienced surgeon.

Long-term endocrinological follow-up evaluation in 115 patients who underwent transsphenoidal surgery for acromegaly was done by Freda et al[13] from 1981 to 1995. This series showed, based on IGF—I measurements and strict GH supression criteria to define remission, that transsphenoidal surgery provides an excellent chance for long-term cure in patients with microadenomas. Surgery alone is successful in most patients with noninvasive macroadenomas; however, most patients with invasive macroadenomas will require adjunctive therapy. Recurrences are uncommon when biochemical remission is clearly documented postoperatively.

Determinants of clinical outcome and survival in acromegaly patients was also studied by Rajsoorya et al[14]. They included one hundred and fifty-one patients (63 females and 88 males) with acromegaly or gigantism treated between the years 1964 and 1989. Patients had their age, estimated duration of symptoms preceding diagnosis, serum GH at diagnosis, presence of diabetes mellitus, cardiovascular disease, hypertension and/or osteoarthritis at diagnosis and the last known serum GH documented. The final outcome at the time of study was graded under three classes: dead ($n = 32$), those with major complications ($n = 47$) and those with minor/no complications ($n = 67$). The mean age at diagnosis of acromegaly was 41 years and the average estimated duration of symptoms prior to diagnosis was 7 years, with older patients showing longer duration of symptoms preceding diagnosis ($P= 0.0002$). Final outcome (dead, alive with major complications, alive and well) was significantly worse in those with older age at diagnosis ($P= 0.008$), longer duration of symptoms before diagnosis ($P= 0.03$) and higher GH at last follow-up ($P= 0.0001$). In multivariate analysis, survival was significantly influenced by the last known GH ($P = 0.0001$), presence of hypertension ($P = 0.02$) or cardiac disease ($P = 0.03$) at diagnosis, and duration of symptoms prior to diagnosis ($P = 0.04$).

Survival in the acromegalic group, irrespective of treatment, was reduced by an average of 10 years compared with the non-acromegalic population. So they concluded that acromegaly had a significant adverse effect on well-being and survival. The predominant determinant of

outcome was the final serum GH level following treatment.

Limitations

The retrospective nature of the study is its limitation.

Conclusion

To conclude, our retrospective study on one hundred and twenty nine patients with acromegaly states that the outcome of these patients is affected by the preoperative size of tumour, intraoperative blood loss, intraoperative complications, duration of surgery and anaesthesia, total fentanyl consumption and duration of postoperative mechanical ventilation in terms of prolonged ICU stay while duration of symptoms, preoperative size of the tumour, duration of surgery and anaesthesia, postoperative mechanical ventilation and ICU stay prolonged the total hospital stay. Postoperative complications were also significantly associated with prolonged ICU stay and hospital stay.

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