Sys Rev Pharm 2019;10(2):104-108
A multifaceted review journal in the field of pharmacy

QUALITY OF LIFE OF PATIENTS TREATED FOR HORMONALLY ACTIVE PITUITARY ADENOMA

Dyussembekov Yermek Kavtaevich, Dossanova Ainur Kassimbekovna, Bazarbekova Rimma Bazarbekovna
JSC Kazakh Medical University of Continuous Education

Article History: *Submitted: 13.08.2019* *Revised: 17.10.2019* *Accepted: 20.11.2019*

ABSTRACT

Adenomas of the pituitary gland represent the most frequent tumors of the chiasmal-sellar region and takes 18% of all brain tumors [1, 22, 25]. Despite the fact that pituitary gland adenomas are benign, 25-55% of them have an invasive growth character, penetrating into surrounding structures [2-4], which undoubtedly affects the quality of their lives. The aim was to study the quality of life of patients receiving various types of therapy for hormonally active adenoma of the pituitary gland (prolactinoma, somatotropinoma, corticotropinoma). We examined 240 patients in dispensary for hormonally active adenoma of the pituitary gland in Almaty polyclinics. Patients with prolactinomas (66.7%), a quarter of patients with somatotropinomas (25%) and the least number of patients with corticotropinomas (8.3%) were frequently examined. Patients with prolactinomas were overwhelmingly on monotherapy with Kabergolin (63.1%), while the rest (36.9%), apart from drug therapy, were subjected to transnasaladenomectomy. All patients with somatotropinomas and corticotropinomas were operated on by trans-nazal trans-sfenoidaladenomectomy.

Medication and radiotherapy were used as additional therapies. The ASBQ questionnaire was used to evaluate the quality of life in patients with hormonally active pituitary adenoma. In general, quality of life in patients with prolactinomas was significantly higher than in other patients.

Quality of life before surgery in patients with somatotropinomas was significantly higher but in dynamics in 1-3 months and several years after the operation the condition of patients with acromegaly was significantly higher than others.

Key words: hormonally active adenoma of the pituitary gland, quality of life, somatotropinoma, prolactinoma, corticotropinoma.

Correspondence:
Dyussembekov Yermek Kavtaevich,
Dossanova Ainur Kassimbekovna,
Bazarbekova Rimma Bazarbekovna
JSC Kazakh Medical University of Continuous Education
Email: ak.dossanova@gmail.com

DOI: 10.5530/srp.2019.2.17

INTRODUCTION

Adenomas of the pituitary gland represent the most frequent tumors of the chiasmal-sellar region and account for 18% of all brain tumors. Prolactinomas and hormonally inactive tumors of the pituitary gland are the most common among all adenomas of the pituitary gland (35%), followed by somatotropinomas (13-15%), corticotropinomas (8-10%), gonadotropinomas (7-9%) and thyreotropinomas (1%), as well as mixed forms [18, 21, 25].

Despite the fact that pituitary adenomas are benign neoplasms, 25-55% of them have an invasive growth character, penetrating into the surrounding structures (sinus of the main bone, cavernous sinus, etc.) [5, 8, 9, 12], which undoubtedly affects the health of patients and reduces their quality of life.

Wide introduction into practice in the treatment of hormonal-active adenoma of the pituitary glandular transfenoidadenomectomy has led to improved surgical outcomes and increased quality of life in patients with this pathology. Thus, according to the data of Borg A. with co-authors, the analysis of the Ovid MEDLINE database (from 1950 to 25 August 2015) revealed 82 studies including 7460 cases in which the frequency of postoperative complications in patients with transasal access was reduced [13-16].

Several parameters are usually used to judge about quality of life: psychological, social, physical, and spiritual well-being. There are no universally applicable criteria and norms for CS research. The basic tool for conducting a quality of life study is questionnaires specially designed for each section of medicine.

Various questionnaires, one of which is the Anterior Skull Base Questionnaire (ASBQ), are used to assess the quality of life of patients with skull base tumors. It is highly valid and easy to use [14, 19, 23]. Based on the foregoing, the aim of our work was to study the quality of life of patients receiving various types of therapies for hormonally active pituitary adenoma (prolactinoma, somatotropinoma, corticotropinoma).

MATERIALS AND METHODS

We examined 240 patients registered in the dispensary for hormonally active adenoma of the pituitary gland in the polyclinics of Almaty. Figure 1 shows the distribution of patients by type of pituitary adenome and treatment methods.

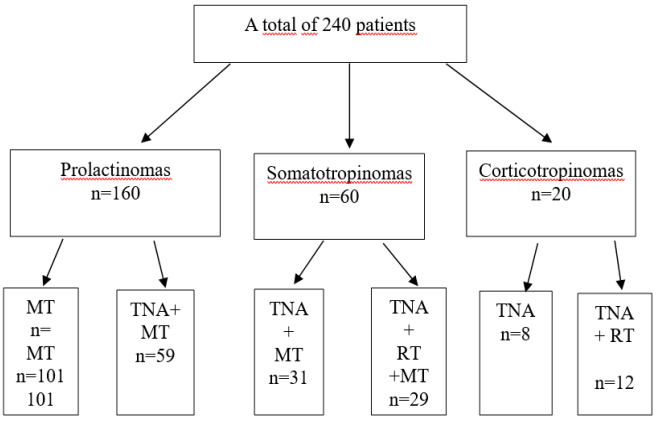

Figure 1. Study design

TNA - transnazaladenomectomy
MT - medication therapy
RT – radiotherapy

As can be seen from Fig. 1, a large number of patients with prolactinomas (160/66.7%), a quarter of patients with somatotropinomas (60/25%) and the least number of patients with corticotropinomas (20/8.3%) were frequently examined.

Patients with prolactinomas were overwhelmingly on monotherapy with Kabergolin (101/63.1%), while the rest (59/36.9%), in addition to drug therapy, were subjected to transnazaladenomectomy due to the development of neurological and/or ophthalmological complications of the underlying disease.

All patients with somatotropinomas were operated on by transnazaltranssfenoidaladenomectomy using a neuronavigator

followed by treatment with somatostatin analogues. Due to the lack of sufficient suppression of somatotropic hormone secretion, radiation therapy (RT) was used as an additional treatment in 29/48.3% of patients. The remaining patients who did not receive RT continued to receive somatostatin analogues for various reasons (31/51.7%).

As for the patients with corticotropinomas, all of them were subjected to a transnazaladenomectomy using a neuronavigator. Due to the lack of ACTH suppression, 12/60% of patients received RT, while the remaining 8/40% did not receive any therapy for various reasons (Fig. 1).

AP was most often detected in young and mature patients. The frequency of pituitary gland adenoma was more than three times higher among women in all age groups than among men (Tables 1-3).

Among patients with prolactinomas, women of reproductive age prevailed at 105/84.7%. Patients aged 40-59 years made up the largest number of male patients - 27/75% (Table 1).

Table 1. Sex-age composition of patients with prolactinomas

Prolactinoma						
Age	Patients' distribution by sex					
	Man		Woman		Both sex	
	Abs	%	Abs	%	Abs	%
Up to 20	0	-	12	9,7	12	7,5
20-29	5	13,9	23	18,5	28	17,5
30-39	3	8,3	48	38,7	51	31,9
40-49	12	33,3	34	27,4	46	28,8
50-59	15	41,7	5	4,1	20	12,5
Above 60	1	2,8	2	1,6	3	1,8
Total	36	100	124	100	160	100

Table 2 shows the prevalence of women with somatotropinomas (44/73.3%) over men of 16/26.0%. Somatotropinomas were most common at the age of 30-59 years. Among women of this age there were 33/75% of patients, among men - 13/81.2%.

Table 2. Sex-age composition of operated patients with somatotropnomas

Somatotropinomas						
Age	Patients' distributionbysex					
	Women 44/73,3%		Men 16/26,7%		Both sex	
	Абс	%	Абс	%	Абс	%
Up to 20	0	0	1	6,3	1	1,7
20-29	7	15,9	2	12,5	9	15
30-39	10	22,7	4	25,0	14	23,3
40-49	8	18,2	5	31,3	13	21,7
50-59	15	34,1	4	25,0	19	31,7
Above 60	4	9,1	0	0	4	6,6
Total	44	100	16	100	60	100%

As shown in Table 3, the majority of those surveyed with corticotropinomas were women (85.7%). About half of them were between the ages of 20 and 29, and 17.6% each were between the ages of 16-20 and 30-39. Among men, 66.7% were patients aged 30-39 years. Thus, the vast majority of those observed were of the most working age.

Table 3. Sex-age composition of operated patients with corticotropinomas

Corticotropinomas						
Age	Patients' distributionbysex					
	Men -14,3%		Wmen-85,7%		Both sex	
	Abc	%	Abc	%	Abc	%
18- 20	0	0	3	17,6	3	15
20-29	0	0	8	47,1	8	40
30-39	2	66,7	3	17,6	5	25
40-49	0	0	2	11,8	2	10
50-59	0	0	1	5,9	1	5
Above 60	1	33,3	0	0	1	5
Total	3	100	17	100	20	100

To evaluate the quality of life of patients with hormonally active pituitary adenomas, the ASBQ questionnaire was used, which consists of 6 blocks of questions aimed at evaluating the various components of a patient's life, such as productivity, endurance, physical activity, endurance, pain, emotions and specific symptoms. Answers to the questions in each block were scored on a five-point Likert scale, with a 1-minimal, 5-minimum score. The higher the sum of points, the higher the Quality of life score of the interviewed patients.

The questionnaire was completed three times: before the operation/beginning of the medication treatment, 1-3 months after the operation/beginning of the medication treatment and several years after the operation/beginning of the medication treatment. The latter was different for patients with different AHs and was between 1 and 3 years (median of 22 months) for patients with prolactinomas, between 1 and 6 years (median of 23 months) for patients with somatotropinomas, between 1 and 6 years (median of 28 months) for patients with corticotropinomas. In some cases, the ASBQ questionnaire was completed in a catamnestic manner, in others by direct interview (Table 4).

Table 4. Dates and methods of filling in the ASBQ questionnaires in patients with pituitary hormonally active adenoma

Questionnaire filling method / Adenoma type	Before surgery/beginning of treatment		In 1-3 months.		Inseveralyears	
	Catamnestically.	Directinterview	Catamnestically.	Directsurvey	Catamnestically.	Directsurvey
Prolactinoma	24/15%	136/85%	22/13%	138/86,3%	-	160/100%
Somatotropinoma	46/76,7%	14/23,3%	44/73,3%	16/26,7%	-	60/100%
Corticotropinoma	18/90%	2/10%	8/40%	12/60%	-	20/100%

Methods of statistical data processing include correlation analysis with χ2 determination to detect correlation between morbidity, sex and age of patients.

A nonparametric Kraskel-Wallis dispersion analysis was used to compare unrelated groups. Paired comparison of groups of patients was performed using Mann-Whitney U-test. Statistically significant was considered $p<0.05$.

RESULTS

The analysis of the obtained data revealed that Quality of life in patients with prolactinomas before the operation was significantly higher than in patients with somatotropinomas (acromegaly). After 1-3 months, a higher level of skin contact was observed in patients with prolactinomas according to the parameters of pain and emotion. A few years after the operation, a significantly higher Quality of life of the patients with prolactinomas was preserved in comparison with the patients with acromegaly in all parameters (Table 5).

Table 5. Comparison of data from patients with prolactinomas and acromegaly according to the ABSQ Mann-Whitney questionnaire

Quality of life evaluation period / Blocks	Beforesurgery/start of treatment (p_1)	In 1-3 monthsaftersurgery/ start of treatment (p_2)	In several months after surgery / start of treatment (p_3)
Productivity	0,007	0,773	0,009
Physicalactivity	0,0001	0,721	0,046
Endurance	0,0001	0,073	0,0001
Paim	0,0001	0,025	0,0001
Emotions	0,0001	0,005	0,0001
Specificsymptoms	0,0001	0,629	0,0001

p1 - when comparing the data of patients with prolactinoma and somatotropinoma before surgery/beginning of treatment

p2 - when comparing the data of patients with prolactinoma and somatotropinoma 1-3 months after the operation/beginning of treatment

p3 - when comparing the data of patients with prolactinoma and somatotropinoma several years after the operation/beginning of treatment

Comparison of the parameters of patients with prolactinomas and corticotropinomas revealed significantly higher Quality of life of patients with prolactinomas in all six parameters both before the operation and in 1-3 months and several years after it (Table 6).

Table 6. Comparison of patient data with prolactinomas and Cushing's disease according to the ABSQ Mann-Whitney questionnaire

Quality of life evaluation period / Blocks	Beforesurgery/ start of treatment (p_1)	In 1-3 monthsaftersurgery/ start of treatment (p_2)	In several months after surgery/ start of treatment (p_3)
Productivity	0,0001	0,006	0,0001
Physicalactivity	0,0001	0,001	0,0001
Endurance	0,014	0,0001	0,0001
Paim	0,0001	0,0001	0,0001
Emotions	0,0001	0,0001	0,0001
Specificsymptoms	0,0001	0,0001	0,0001

p1 - when comparing the data of patients with prolactinoma and Cushing's disease before surgery/beginning of treatment

p2 - when comparing the data of patients with prolactinoma and Cushing's disease 1-3 months after the operation/beginning of treatment

p3 - when comparing the data of patients with prolactinoma and Cushing's disease several years after the operation/beginning of treatment

A comparative assessment of Quality of life in acromegaly and Cushing's disease patients showed that before Quality of life in somatotropinoma patients was higher in all but two parameters - emotions and specific symptoms. Later, after 1-3 months and several years, the condition of patients with acromegaly was significantly higher than that of Cushing's disease (Table 7).

Table 7. Comparison of data from acromegaly and Cushing's disease patients according to the ABSQ Mann-Whitney questionnaire

Quality of life evaluation period / Blocks	Beforesurgery/ start of treatment (p_1)	In 1-3 monthsaftersurgery/ start of treatment (p_2)	In several months after surgery/ start of treatment (p_3)
Productivity	0,0001	0,018	0,0001
Physicalactivity	0,015	0,006	0,002
Endurance	0,0001	0,0001	0,004
Paim	0,001	0,003	0,0001
Emotions	0,741	0,0001	0,003
Specificsymptoms	0,732	0,0001	0,029

p1 - when comparing data from patients with acromegaly and Cushing's disease before surgery

p2 - when comparing the data of patients with acromegaly and Cushing's disease 1-3 months after surgery

p3 - when comparing data from patients with acromegaly and Cushing's disease several years after surgery

DISCUSSION

As a result of our study it was found out that the Quality of life in patients with prolactinomas was significantly higher in all time intervals than in patients with acromegaly and Cushing's disease.

Quality of life in acromegaly patients was higher than in Cushing's disease patients in all cases except for emotional parameters and specific symptoms. In dynamics in 1-3 months and several years after the operation the condition of patients with acromegaly was significantly higher than that of patients with Cushing's disease in all parameters.

The data obtained can be explained by the fact that remission in the treatment of patients with acromegaly and Cushing's disease is not always possible [15-18].

In the case of prolactin treatment, good results have been achieved to date. Thus, according to L.K. Dzeranova, the use of cabergoline in the treatment with prolactin leads to normalization of the level of prolactin in women in 70%, restoration of the menstrual cycle in reproductive age in 16.1%, stopping of galactorrhea in 63%; in men - in 86%, restoration of impaired sexual functions in 65% of cases [6,8].

Similar data were obtained in a cross-sectional study in which 278 patients with pituitary gland adenomas (n=81 acromegaly, n=45 NIR, n=92 prolactinoma, n=60 Cushing's disease) were evaluated. Pain was studied using questionnaires to screen for nociceptive and neuropathic pain components (pain DETECT), to determine the severity of pain, quality, duration, location, and to assess the impact of pain on disability (assessment of disability in migraine, MIDAS) and CSF. High prevalence of body pain (n = 180/65%) and headache (n = 178/64%) was reported. It is important to note that corticotropinomas were more likely to have various localizations (n = 34/76%). Headache was equally frequent in patients with macro- and microadenomas (68 vs. 60%, p=0.266). According to pain DETECT, most patients had a nociceptive pain component (n = 193/80%). Despite the high prevalence of headache, 72% reported little or no headache-related disability (MIDAS). Neuropathic pain and pain-related disability correlated with depression and QI impairment [17-20].

In addition, acromegaly and Cushing's disease are often treated with radiation therapy, which cannot but have a negative impact on the brain. In particular, radiation therapy often leads to the development of hypopituitarism, damage to the optic nerves, seizures, and radial necrosis of the brain tissue. Nikitya K.V. has shown that radiotherapy for intranranial volumetric formations is fraught with the risk of radiation damage to the brain, which can be manifested in the form of necrosis sites in different parts of the brain and other morphological changes in tissues, such as perivascular fibrosis, telangiectasia, thrombosis and haemorrhage [8].

CONCLUSIONS

1. In general, Quality of life in patients with prolactinomas was significantly higher in all time intervals than in patients with acromegaly and Cushing's disease.

2. Quality of life before surgery in patients with somatotropinomas was significantly higher than in patients with corticotropinomas on all indicators, except for the parameters of emotion and specific symptoms. In dynamics in 1-3 months and several years after the operation the condition of patients with acromegaly was significantly higher than that of patients with NIC on all parameters.

REFERENCES

1. Zhestikova M.G., KanYa.A., Sholomov I.I. Modern methods of treatment of pituitary adenoma // Saratov Scientific Medical Journal. 2011. T. 7, № 1. p. 112-114.
2. Fomichev D, Kalinin P, Kutin M, Sharipov O. Extended Transsphenoidal Endoscopic Endonasal Surgery of Suprasellar Craniopharyngiomas. World Neurosurgery [Internet]. Elsevier BV; 2016 Oct;94:181–7. Available from: http://dx.doi.org/10.1016/j.wneu.2016.06.124
3. Borg A, Kirkman MA, Choi D. Endoscopic Endonasal Anterior Skull Base Surgery: A Systematic Review of Complications During the Past 65 Years. World Neurosurgery [Internet]. Elsevier BV; 2016 Nov;95:383–91. Available from: http://dx.doi.org/10.1016/j.wneu.2015.12.105
4. Kadasheva AB, Cherekaev VA, Shifrin MA, Kozlov AV, Gol'bin DA, Tsukanova TV, et al. Life quality of patients with benign tumors of the anterior and middle part of the skull base after surgery and during follow-up. Voprosy neirokhirurgii imeni NN Burdenko [Internet]. Media Sphere Publishing Group; 2015;79(2):44. Available from: http://dx.doi.org/10.17116/neiro201579244-54
5. GrigorievA.Yu. Neurosurgical treatment of patients with Itzenko-Cushing's disease and acromegaly: author's abstract of doctoral thesis - M, 2011. - 35 p.
6. Dzeranova L.K. Hyperprolactinemia Syndrome in Women and Men: Clinic, Diagnostics, Treatment : Abstract Dissemination ... Doctor of Medical Sciences - Moscow, 2007. - 54 p.
7. Dimopoulou C, Athanasoulia AP, Hanisch E, Held S, Sprenger T, Toelle TR, et al. Clinical characteristics of pain in patients with pituitary adenomas. European Journal of Endocrinology [Internet]. Bioscientifica; 2014 Nov;171(5):581–91. Available from: http://dx.doi.org/10.1530/eje-14-0375
8. Nikitin, K.V. Local brain radiation damage after radiotherapy and radiosurgery of intrarranial volumetric formations: autoref. - – M., 2010. - – 24 p.
9. Penner F, Prencipe N, Pennacchietti V, Pacca P, Cambria V, Garbossa D, et al. Super Giant Growth Hormone–Secreting Pituitary Adenoma in Young Woman: From Ventricles to Nose. World Neurosurgery [Internet]. Elsevier BV; 2019 Feb;122:544–8. Available from: http://dx.doi.org/10.1016/j.wneu.2018.11.069
10. Solari D, Pivonello R, Caggiano C, Guadagno E, Chiaramonte C, Miccoli G, et al. Pituitary Adenomas: What Are the Key Features? What Are the Current Treatments? Where Is the Future Taking Us? World Neurosurgery [Internet]. Elsevier BV; 2019 Jul;127:695–709. Available from: http://dx.doi.org/10.1016/j.wneu.2019.03.049
11. Webb SM, Martínez-Momblán MA, Resmini E, Valassi E, Santos A. Quality of life in patients with pituitary tumors. Current Opinion in Endocrine and Metabolic Research [Internet]. Elsevier BV; 2018 Aug;1:67–73. Available from: http://dx.doi.org/10.1016/j.coemr.2018.02.004
12. Van Beek AP, van den Bergh ACM, van den Berg LM, van den Berg G, Keers JC, Langendijk JA, et al. Radiotherapy is Not Associated With Reduced Quality of Life and Cognitive Function in Patients Treated for Nonfunctioning Pituitary Adenoma. International Journal of Radiation Oncology*Biology*Physics [Internet]. Elsevier BV; 2007 Jul;68(4):986–91. Available from: http://dx.doi.org/10.1016/j.ijrobp.2007.01.017
13. Crespo I, Webb SM. Health-Related Quality of Life and Behavior in Patients with Both Pituitary and Hypothalamic Diseases. Hormones, Brain and Behavior [Internet]. Elsevier; 2017;343–54.

Available from: http://dx.doi.org/10.1016/b978-0-12-803592-4.00083-3

14. Crespo I, Valassi E, Santos A, Webb SM. Health-Related Quality of Life in Pituitary Diseases. Endocrinology and Metabolism Clinics of North America [Internet]. Elsevier BV; 2015 Mar;44(1):161–70. Available from: http://dx.doi.org/10.1016/j.ecl.2014.10.013
15. Cuny T, Barlier A, Feelders R, Weryha G, Hofland LJ, Ferone D, et al. Medical therapies in pituitary adenomas: Current rationale for the use and future perspectives. Annales d'Endocrinologie [Internet]. Elsevier BV; 2015 Feb;76(1):43–58. Available from: http://dx.doi.org/10.1016/j.ando.2014.10.002
16. Robertson J, Brandão J, Blas-Machado U, Cohen E, Mayer J. SPONTANEOUS PANCREATIC ISLET CELL ADENOMA WITH PERIPHERAL NEUROPATHY IN A PET RAT (RATTUS NORVEGICUS). Journal of Exotic Pet Medicine [Internet]. Elsevier BV; 2019 Jan;28:166–72. Available from: http://dx.doi.org/10.1053/j.jepm.2018.10.003
17. Sauer N, Flitsch J, Doeing I, Dannheim V, Burkhardt T, Aberle J. Non-functioning pituitary macroadenomas: Benefit from early growth hormone substitution after surgery. Growth Hormone & IGF Research [Internet]. Elsevier BV; 2014 Apr;24(2-3):71–5. Available from: http://dx.doi.org/10.1016/j.ghir.2014.03.001
18. McCord MW, Buatti JM, Fennell EM, Mendenhall WM, Marcus RB, Rhoton AL, et al. Radiotherapy for pituitary adenoma: Long-term outcome and sequelae. International Journal of Radiation Oncology*Biology*Physics [Internet]. Elsevier BV; 1997 Sep;39(2):437–44. Available from: http://dx.doi.org/10.1016/s0360-3016(97)00335-0
19. Cross E, Moreland R, Wallack S. Feline Pituitary-Dependent Hyperadrenocorticism and Insulin Resistance Due to a Plurihormonal Adenoma. Topics in Companion Animal Medicine [Internet]. Elsevier BV; 2012 Feb;27(1):8–20. Available from: http://dx.doi.org/10.1053/j.tcam.2011.12.001
20. Anna Maria Formenti, Filippo Maffezzoni, auro Doga, Growth hormone deficiency in treated acromegaly and active Cushing's syndrome Best Practice & Research Clinical Endocrinology & Metabolism, Volume 31, Issue 1, February 2017, Pages 79-90. Available from: https://doi.org/10.1016/j.beem.2017.03.002
21. Sauer N, Flitsch J, Doeing I, Dannheim V, Burkhardt T, Aberle J. Non-functioning pituitary macroadenomas: Benefit from early growth hormone substitution after surgery. Growth Hormone & IGF Research [Internet]. Elsevier BV; 2014 Apr;24(2-3):71–5. Available from: http://dx.doi.org/10.1016/j.ghir.2014.03.001
22. Cuny T, Barlier A, Feelders R, Weryha G, Hofland LJ, Ferone D, et al. Medical therapies in pituitary adenomas: Current rationale for the use and future perspectives. Annales d'Endocrinologie [Internet]. Elsevier BV; 2015 Feb;76(1):43–58. Available from: http://dx.doi.org/10.1016/j.ando.2014.10.002
23. Colin P, Jovenin N, Delemer B, Caron J, Grulet H, Hecart A-C, et al. Treatment of pituitary adenomas by fractionated stereotactic radiotherapy: A prospective study of 110 patients. International Journal of Radiation Oncology*Biology*Physics [Internet]. Elsevier BV; 2005 Jun;62(2):333–41. Available from: http://dx.doi.org/10.1016/j.ijrobp.2004.09.058
24. Crespo I, Valassi E, Santos A, Webb SM. Health-Related Quality of Life in Pituitary Diseases. Endocrinology and Metabolism Clinics of North America [Internet]. Elsevier BV; 2015 Mar;44(1):161–70. Available from: http://dx.doi.org/10.1016/j.ecl.2014.10.013
25. Cordido F, García Arnés JA, Marazuela Aspiroz M, Torres Vela E. Practical guidelines for diagnosis and treatment of acromegaly. Endocrinología y Nutrición (English Edition) [Internet]. Elsevier BV; 2013 Oct;60(8):457.e1–457.e15. Available from: http://dx.doi.org/10.1016/j.endoen.2013.10.012