

Guidelines for Acromegaly Management: An Update

S. Melmed, A. Colao, A. Barkan, M. Molitch, A. B. Grossman, D. Kleinberg, D. Clemmons, P. Chanson, E. Laws, J. Schlechte, M. L. Vance, K. Ho, and A. Giustina

Department of Medicine (S.M.), Cedars-Sinai Medical Center, Los Angeles, California 90048; Department of Molecular and Clinical Endocrinology and Oncology (A.C.), Federico II University of Naples, 80138 Naples, Italy; Division of Endocrinology and Metabolism (A.B.), University of Michigan Medical Center, Ann Arbor, Michigan 48109; Endocrinology Clinic (M.M.), Feinberg School of Medicine, Northwestern University, Chicago, Illinois 60611; Department of Endocrinology (A.B.G.), St. Bartholomew's Hospital, London EC1A 7BE, United Kingdom; Department of Medicine (D.K.), New York University Medical Center, New York, New York 10016; Division of Endocrinology (D.C.), University of North Carolina, Chapel Hill, North Carolina 27599; Assistance Publique-Hôpitaux de Paris (P.C.), Department of Endocrinology and Reproductive Diseases, Hôpital de Bicêtre and Université Paris-Sud 11, Le Kremlin-Bicêtre F-94276, France; Department of Neurosurgery (E.L.), Brigham & Women's Hospital, Boston, Massachusetts 02115; Department of Internal Medicine (J.S.), University of Iowa, Iowa City, Iowa 52242; Department of Medicine (M.L.V.), University of Virginia, Charlottesville, Virginia 22904; Pituitary Research Unit (K.H.), Garvan Institute of Medical Research, Sydney NSW 2010, Australia; and Department of Internal Medicine (A.G.), University of Brescia, 25121 Brescia, Italy

Objective: The Acromegaly Consensus Group reconvened in November 2007 to update guidelines for acromegaly management.

Participants: The meeting participants comprised 68 pituitary specialists, including neurosurgeons and endocrinologists with extensive experience treating patients with acromegaly.

Evidence/Consensus Process: Goals of treatment and the appropriate imaging and biochemical and clinical monitoring of patients with acromegaly were enunciated, based on the available published evidence.

Conclusions: The group developed a consensus on the approach to managing acromegaly including appropriate roles for neurosurgery, medical therapy, and radiation therapy in the management of these patients. (*J Clin Endocrinol Metab* 94: 1509–1517, 2009)

The Acromegaly Consensus Group has produced several consensus documents on various aspects of acromegaly management since 2000 (1–5). In 2002, the group published comprehensive guidelines for acromegaly management (2), and in November 2007 the group reconvened to update these guidelines. The participants in this sixth meeting of the Consensus Group, sponsored by the Pituitary Society and the European Neuroendocrine Association, developed a consensus and provided a new set of recommendations on acromegaly management that reflect the current knowledge in 2007.

Recommendations were graded, based on the GRADE system (6, 7), depending on the quality of evidence as very low quality (VLQ) expert opinion with one or a small number of uncontrolled studies in support, low quality (LQ) large series of uncontrolled studies, moderate quality (MQ) one or a small num-

ber of large uncontrolled studies or meta-analyses, or high quality (HQ) controlled studies or large series of large uncontrolled studies with sufficiently long follow-up. Recommendations were classed as discretionary recommendations (DR) if based on VLQ or LQ evidence and as strong recommendations (SR) if based on MQ and HQ evidence.

Clinical Background

Although the pituitary tumors associated with acromegaly are nearly always benign, the elevated GH and IGF-I levels lead to a wide range of cardiovascular, respiratory, endocrine, and metabolic morbidities (8, 9). These can range in severity from subtle signs of acral overgrowth or soft-tissue swelling to diabetes and

cardiac failure. Symptoms from an expanding tumor, such as visual-field defects and headache, might accompany the clinical presentation of acromegaly.

In a recent meta-analysis, the weighted mean of the standardized mortality ratio (SMR) from 16 published studies of patients with acromegaly was 1.72 [95% confidence interval (CI), 1.62–1.83] (10) MQ. A meta-regression analysis demonstrated improved survival in more recent studies, presumably due to modern treatment modalities (including transsphenoidal surgery) and more strictly defined cure criteria, but even in recent studies there was a 32% increased risk for all-cause mortality in patients with acromegaly (10). Patients with random serum GH level below 2.5 ng/ml after treatment, mostly measured by standard RIA, had mortality close to expected levels [SMR, 1.1 (95% CI, 0.9–1.4), compared with a SMR of 1.9 (95% CI, 1.5–2.4) for those with a final GH level > 2.5 ng/ml] (11). Similarly, a normal serum IGF-I level for age and sex at last follow-up after treatment was associated with an SMR of 1.1 (95% CI, 0.9–1.4) compared with an SMR of 2.5 (95% CI, 1.6–4.0) for those with elevated IGF-I levels (11) MQ. There was a significant trend for reduced mortality in series reporting frequent use of somatostatin receptor ligands (SRLs) and in studies reporting high rates (>70%) of biochemical remission after treatment (11). In cases where GH and IGF-I results are divergent, it is important to consider the degree of the biochemical abnormality and the clinical context before initiating further therapy (12–14).

Therapies for acromegaly have the aim of reducing or controlling tumor growth, inhibiting GH hypersecretion, and normalizing IGF-I levels. The three approaches to therapy are surgery, medical management, and radiotherapy. Each treatment modality has specific advantages and disadvantages, but the optimal use of these treatments should result in a reduction in mortality in the acromegaly patient population compared to that of the general population. However, conventional fractionated radiotherapy may be associated with increased mortality (13, 15) LQ.

The goal of the Acromegaly Consensus Group meetings is to ensure that patients with acromegaly receive optimal treatment by creating a common understanding of best practice among endocrinologists, neurosurgeons, and radiotherapists. This manuscript presents the consensus on the optimal use of management modalities in patients with acromegaly.

The Role of Neurosurgery

Complete surgical removal of GH-secreting tumors results in hormonal control of acromegaly and improvement of soft tissue changes.

Transsphenoidal surgery is the treatment of choice for intrasellar microadenomas, noninvasive macroadenomas (*i.e.* those without cavernous sinus or bone invasion), and when the tumor is causing compression symptoms. In patients with intrasellar microadenomas, surgical removal provides biochemical control with normalization of IGF-I in 75–95% of patients (16–21) HQ. Control rates are lower in patients with noninvasive macroadenomas, but even in these cases surgical removal provides bio-

chemical control with normalization of IGF-I in 40–68% of patients (16–21). The exact influence of tumor size on surgical outcome is still uncertain. However, as a preliminary guideline, a tumor at least 2 cm in diameter is associated with a greatly reduced success rate (20) HQ. Craniotomy is very rarely indicated in patients with acromegaly.

Expertise in surgical management of acromegaly is very important—the control rates outlined above can only be achieved when surgery is performed by a dedicated and experienced pituitary neurosurgeon conducting at least 50 pituitary operations per year (22–24). Lower control rates in some published papers almost certainly reflect the level of experience of the surgeon(s) involved. In addition, a skilled multimodality team, either in a multidisciplinary center or via a network or virtual team, is required for optimal surgical results. Such a team should include the experienced surgeon using advanced surgical techniques, an endocrinologist with pituitary expertise, and a physician with radiotherapy expertise.

Newer surgical adjuncts such as computerized navigation, endoscopy, and intraoperative magnetic resonance imaging (MRI) may be used with (or instead of) standard equipment, but such decisions depend on the preference of the surgeon. The current evidence on the use of newer endoscopic surgical techniques is promising but limited; more research is needed (25).

In experienced hands, complications of transsphenoidal surgery in acromegaly are rare, including transient oculomotor palsies, deterioration of vision, carotid artery injury, and epistaxis (occurring in less than 1% of patients) (17, 18), and therefore safety can only be marginally improved with new surgical developments (17, 18, 26).

Contraindications to surgery include patient refusal, severe cardiomyopathy or respiratory disease, or the lack of an available skilled surgeon.

Presurgical treatment

In many studies, the effects of presurgical treatment with a SRL on surgical outcome and postoperative complications have been assessed (27–30). Some authors have concluded that pretreatment with a SRL can improve normalization of GH and IGF-I after surgery and shorten the duration of hospitalization (27), whereas others have found no benefits to SRL pretreatment (28) VLQ. Medical treatment before surgery is certainly not contraindicated, but there is currently insufficient evidence to recommend it for improved surgical outcome or postoperative complications (31).

Tumors unlikely to be controlled by surgery

Although transsphenoidal surgery is the treatment of choice for most microadenomas and some macroadenomas, approximately 40–60% of macroadenomas are unlikely to be controlled with surgery alone (for example, tumors with cavernous sinus invasion lateral to the carotid artery or those with transcapsular intracranial invasion). Options for such tumors are discussed in subsequent sections of this document and include primary medical therapy or primary surgical debulking followed by medical therapy for hormonal control and/or radiation therapy for treatment of residual tumor. Recent studies suggest that surgical

debulking may increase the proportion of patients that subsequently achieves GH control and normalized IGF-I with SRL therapy, especially when more than 75% of the tumor is removed (32–34) LQ.

Ongoing challenges

The success of neurosurgery is dependent upon the availability of skilled and experienced surgeons and multimodality teams. However, the availability of the appropriate personnel is variable even in large cities, and in most countries there is an absence of regional networks to guide referral to expert centers.

Tumor staging classification systems have been proposed [for example, Hardy *et al.* (35)], but these are not in widespread use. A modified classification system for defining adenoma size and invasiveness is needed and may increase the use of such systems. This would provide standardized recommendations on identifying which adenomas are suitable targets for surgical removal.

As with all treatment modalities discussed in this statement, there is a need for cost-effectiveness analyses of surgery and of the relative cost-benefit ratio of pretreatment with an SRL or surgical debulking before using other treatment modalities. Specific cost-effectiveness studies may resolve these issues.

The Role of Medical Therapy

Currently, there are three drug classes available for the treatment of acromegaly: dopamine agonists (DAs), SRLs, and a GH receptor antagonist (GHRA). For women who become pregnant while on medical therapy, cessation of medical therapy during pregnancy is usually advised, primarily based on the lack of a large database demonstrating the safety of such use.

Somatostatin receptor ligands

The SRLs signal predominantly via somatostatin receptor subtypes 2 and 5 (36), leading to a decrease in adenoma GH secretion.

The use of SRLs is most appropriate:

- As first-line therapy when there is a low probability of a surgical cure (for example, large extrasellar tumors with no evidence of central compressive effects) (37–41) DR.
- After surgery has failed to achieve biochemical control SR.
- Before surgery to improve severe comorbidities that prevent or could complicate immediate surgery (the benefits of this are unproven) (42) DR.
- To provide disease control, or partial control, in the time between administration of radiation therapy and the onset of maximum benefit attained from radiation therapy (radiation therapy can take several years to produce disease control—see below) SR.

SRLs are effective in controlling GH/IGF-I hypersecretion and in reducing tumor size. Long-term studies indicate that approximately 70% of patients receiving SRLs have GH levels below 2.5 ng/ml and normalized IGF-I, and maximal benefit may be achieved after 10 yr of therapy (37, 43) MQ. However, these studies often include patients preselected for GH responsivity. In

unselected populations, SRLs reduce GH to less than 2.5 ng/ml and normalize IGF-I in 44 and 34% of patients, respectively (38). Tumor shrinkage of more than 20% occurs in approximately 75% of acromegaly patients receiving these drugs (mean 50% reduction in tumor volume) (39, 44).

These peptide analogs have a proven safety record. Common side effects include abdominal bloating and cramping, with a reduction over the first few months of treatment. Multiple small gallstones and gallbladder sludge commonly occur, but they rarely cause cholecystitis. There have been a small number of cases who have developed pancreatitis with the use of SRLs—a finding that seems paradoxical because of the benefits seen in other settings when these drugs are used to treat pancreatitis.

In well-designed trials, the long-acting formulations of the two SRLs currently available [octreotide LAR and lanreotide Autogel (or Somatuline depot in the United States)] appear to be equivalent in the control of symptoms and biochemical markers in patients with acromegaly (45).

Patients should remain on the same dose for 3 months (assuming the patient tolerates the medication) to properly assess adequacy of treatment and the need for dose titration.

GH receptor antagonist

There is currently a single GHRA available, pegvisomant, for the treatment of acromegaly. The indications for its use are:

- In patients that have persistently elevated IGF-I levels despite maximal therapy with other treatment modalities SR.
- Possibly as monotherapy or in combination with a SRL in other patients DR. However, more data are required before firm guidelines can be given on this.

Pegvisomant is highly effective in acromegaly and significantly improves the quality of life (QoL) in patients that require both SRLs and pegvisomant to achieve biochemical control (46) MQ. Safety issues with GHRA include liver function abnormalities and tumor growth. Tumor growth is infrequent (<2%) (47), and approximately 25% of patients have liver function abnormalities, but these appear to be transient in most patients without changing the GHRA dose (48, 49). Whether the tumor growth is due to the GHRA or merely reflects ongoing tumor growth when there is no therapy directed specifically at the tumor has not been established definitively.

Combination therapy with a SRL and GHRA

Recent publications suggest that GHRA may be useful in combination therapy with a SRL (50–52), but there are no direct comparisons between combination therapy and monotherapy with GHRA. The combination of a SRL and a GHRA may be useful for patients with acromegaly that is resistant to other treatment modalities, for patients who have not achieved biochemical control after surgery, or to improve cost-effectiveness in patients that would otherwise require high-dose GHRA monotherapy.

Dopamine agonist

Of the two DAs, bromocriptine and cabergoline, only cabergoline has any efficacy in acromegaly, and this is limited—mono-

therapy is effective in less than 10% of patients (53–56) VLQ. Clinical situations in which cabergoline may be useful include:

- When the patient prefers oral medication (DAs are the only oral medication available for acromegaly) DR.
- After surgery (very occasionally as first-line therapy) in selected patients, such as those with markedly elevated prolactin and/or modestly elevated GH and IGF-I levels DR.
- As additive therapy to SRL therapy in patients partially responsive to a maximum SRL dose DR—approximately 50% of such patients may achieve control of GH and IGF-I levels with combination therapy LQ (57–62).

There is evidence that in patients with Parkinson's disease, high doses of cabergoline (higher than doses used for the treatment of pituitary tumors), and a prolonged duration of therapy, are associated with the development of cardiac valvular abnormalities. Valvular disease has not been found in patients receiving the conventional doses used for pituitary tumors (63, 64). It would be prudent, however, to monitor patients receiving higher than conventional doses of cabergoline for prolonged periods of time by performing echocardiography.

Control of comorbidities via biochemical control of acromegaly

In addition to medical therapy for GH/IGF-I hypersecretion, treatment of comorbidities has an important impact on QoL and mortality. A number of comorbidities are present in patients with acromegaly, including arthropathy, hypertension, obstructive sleep apnea (OSA), diabetes, cardiomyopathy, colon polyps, goiter, and headache (9, 65). Successful treatment of GH/IGF-I hypersecretion will control these comorbidities to varying degrees, but some may persist in patients even after biochemical control of acromegaly (and some comorbidities may improve even if biochemical control is not achieved) (66). All comorbidities should be actively diagnosed and treated, irrespective of GH and IGF-I control.

Ongoing challenges

There are certain areas where more data are needed on the use of medical therapies in acromegaly. Firstly, there are no head-to-head studies of the different SRLs of adequate design and power to recommend one drug over the other. Secondly, data on the potential use of GHRA as a first-line treatment or in combination with SRLs are needed. And thirdly, the relative cost-effectiveness of all medical therapies as monotherapy, or in the various combination options discussed above, requires evaluation.

The Role of Radiation Therapy

When radiation therapy for acromegaly is being considered, it should be conducted by an experienced pituitary radiotherapist in a specialized center. Radiation therapy should generally be reserved for third-line treatment, occasionally as second-line treatment, but rarely as first-line treatment. Patients who do not have tumor growth control or normalization of hormone levels

with surgery (for example, after debulking of a nonresectable tumor) and/or medical therapy are possible candidates for radiation therapy. Radiation therapy may be useful in patients receiving GHRA (who have failed other medical therapies) and are at risk of tumor expansion. Some endocrinologists may consider radiotherapy in patients controlled on drug therapy to allow for potential termination of such therapy, which would otherwise be lifelong.

Conventional radiotherapy (conformal fractionated radiotherapy) can lower GH levels and normalize IGF-I in over 60% of patients, but maximum response is achieved 10–15 yr after radiotherapy is administered (67–69) HQ. Medical therapy with a SRL is usually required during this latency period. An alternative to conventional radiotherapy is single-dose, focused radiotherapy such as that achieved with the Gamma Knife or Linear Accelerator. Five-year remission rates with gamma knife radiotherapy in patients with acromegaly (after surgical debulking) range from 29 to 60% (70–73) MQ. However, studies of gamma knife radiotherapy suffer from selection bias because only patients with a smaller tumor size are included. No long-term data are currently available for the use of gamma knife radiotherapy in acromegaly.

If radiation therapy is deemed necessary, the choice of technique is dependent upon the tumor characteristics: conventional radiotherapy is preferred for large tumor remnants or tumors that are too close to optic pathways, whereas stereotactic radiotherapy is preferred when there is a smaller tumor size or when improved patient convenience is desired. Stereotactic radiotherapy may produce beneficial effects on GH and IGF-I sooner than conventional radiotherapy, but this is unproven and may be due to the aforementioned selection bias in trials. At present, there is insufficient evidence to provide definitive recommendations in favor of one particular technique over another.

The main limitation to the use of radiation therapy in acromegaly is safety, especially when other safer treatment modalities exist. Hypopituitarism is observed in over 50% of patients receiving radiation therapy, and after 5–10 yr, the incidence is similar with conventional radiotherapy and stereotactic radiotherapy (68, 71–73). The probability of hypopituitarism appears similar with all types of radiotherapy. However, if hypopituitarism is already present in a patient, this is less of an issue. There is also a small but significant risk of vision defects, especially with focal treatment plans—as many as 5.5% of patients could potentially be affected (68, 70, 71, 74). Conventional radiotherapy may carry a risk of second tumors or cerebrovascular events due to radiation vasculopathy (13–15, 75–77), but long-term data on the risk of these events with stereotactic radiotherapy are not yet available.

Ongoing challenges

Many of the potential safety concerns with radiation therapy for acromegaly remain unresolved. The possible causative link between radiation therapy and cerebrovascular mortality and morbidity is still unclear (77). In addition, although second tumors have been reported (76), data on the effects of newer focused radiation therapy techniques on the development of second tumors are not yet available. The reports of second tumors

may relate to an increased incidence of such tumors in patients with a pituitary tumor, or may be the result of more intensive surveillance.

Long-term complications, particularly neurocognitive defects, of radiation therapy require further evaluation, and especially in young patients, the long-term (>30 yr) effects of radiation therapy are unknown.

It is not possible to provide recommendations on the preferred radiation therapy technique for patients with acromegaly. Studies with more homogeneous patient populations would be required to accurately assess the relative efficacy of conventional radiotherapy *vs.* stereotactic radiotherapy.

Goals of Treatment

Mortality reduction

The appropriate use of modern management modalities reduces mortality from acromegaly to the level in the general population. Thus, normalizing mortality in patients with acromegaly is a key aim of disease management. Based on the fact that basal GH levels above 2.5 ng/ml (15, 78), elevated IGF-I (12, 14, 78), age and disease duration (14, 78), hypertension (78), diabetes, and cardiac disease are the main determinants of mortality HQ, biochemical goals to control mortality are a GH less than 2.5 ng/ml or a normal age and sex-adjusted IGF-I level. Comorbidities that are associated with mortality must also be treated appropriately, and because disease duration determines mortality, early diagnosis of acromegaly and prompt treatment are recommended.

Tumor shrinkage

Control of tumor mass, which may impinge on vital central structures, is an essential goal of acromegaly therapy.

The different treatment modalities have different effects on tumor mass. Surgery achieves immediate and substantial debulking, radiotherapy takes years to reduce tumor mass, therapy with GHRA does not induce tumor shrinkage (and in a small proportion of cases may induce tumor growth), and DAs only reduce tumor mass in approximately 5% of patients, whereas SRLs reduce tumor mass more than 20% (on average approximately 50%) in 75% of patients (37–41, 44) MQ. Tumor shrinkage in patients receiving SRLs is independent of age and initial tumor size. There is, in general, a concordance between biochemical and anatomical response, but tumor shrinkage may occur even in the absence of a biochemical response (79). Increased tumor size has not been reported in patients achieving biochemical control except in patients taking GHRAs.

Tumor mass should be monitored with MRI, and the frequency of MRI should be decreased after tumor growth control is established LQ.

Treatment of comorbidities

Hypertension, cardiac dysfunction, diabetes, osteoarthropathy, and OSA are the most important comorbidities of acromegaly and can all lead to significant functional disability (80–86). Surgical removal of pituitary tumors and biochemical control of

acromegaly (by any treatment modality) may reverse or halt progression of these comorbidities in some patients, but a significant proportion will need additional management (84, 87–89). Comorbidities should be managed (that is, treatment of abnormal lipid levels, and elevated glucose and blood pressure, especially to prevent stroke and other cardiovascular problems) and response to treatment monitored, as they would be for the general population with these morbidities LQ.

Some studies have shown that SRLs have a suppressive effect on β -cell function (90) and could potentially decrease insulin secretion VLQ. The reduction in GH levels usually achieved with SRL therapy tends to outweigh any effect on β -cell function and leads to an overall improvement in insulin resistance, but if diabetes control worsens while the patient is on therapy, substituting with a GHRA can be considered.

The incidence of premalignant colonic lesions may be increased in acromegaly (83, 91), and therefore, at diagnosis, all patients should have a colonoscopy SR. Subsequent follow-up investigation should be implemented as in the general population. The evidence for a link between an increased risk of colorectal malignancies and uncontrolled acromegaly is controversial.

Monitoring the Patient with Acromegaly

A regular transparent audit of outcomes and complications [combined surgical and endocrinological (hormonal) follow-up] in all centers managing patients with acromegaly is recommended. To aid such audits, the promulgation of a uniform tumor staging classification system (of size and invasiveness)—for example, the system proposed by Hardy (35)—is needed to standardize monitoring of tumor response.

Biochemical markers of response

Both GH and IGF-I should be measured to assess the biochemical response to any medical treatment SR (except when patients are receiving GHRA therapy, in which case only IGF-I should be measured). Measurement of GH during an oral glucose tolerance test (OGTT; measurement of GH and glucose at 0, 30, 60, and 120 min after glucose load) may be preferred to a random GH measurement and should be performed 3–6 months after surgery. Thereafter, IGF-I, a random GH or GH during an OGTT should be measured at follow-up visits SR. OGTT is not helpful in monitoring therapeutic responses while patients are receiving SRL therapy (92, 93).

Studies of patients with acromegaly have used a number of different treatment endpoints to define response, and therefore, different cutoff values for GH and IGF-I have been suggested. However, biochemical control is generally defined as a normal IGF-I for age and gender and a GH less than 1.0 ng/ml during an OGTT. The cutoff value for GH used within each individual center depends upon the reliability of the assay used and the ability of the laboratory to provide normative data with very high sensitivity assays (92). Using sensitive assays, a GH of less than 0.4 ng/ml would be consistent with remission. Retrospective studies measuring GH using RIA (which is no longer routinely

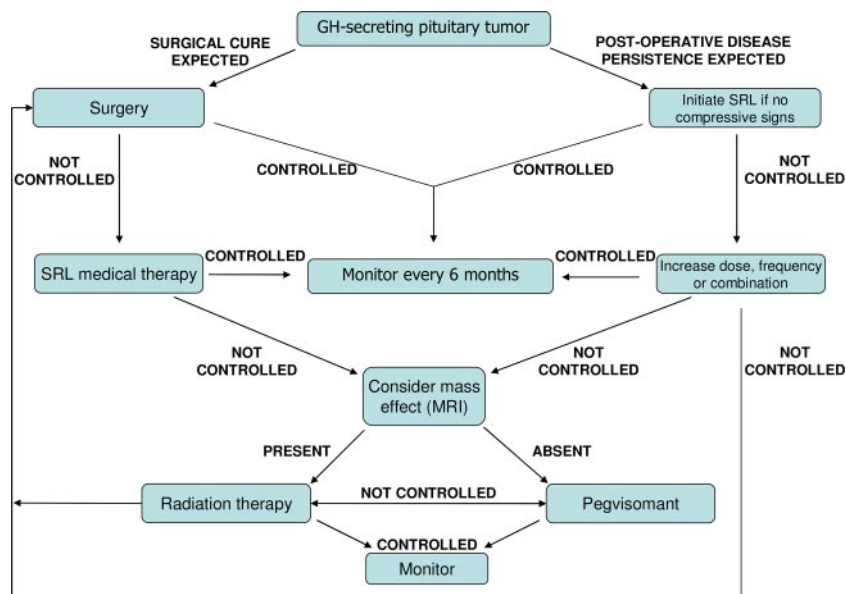


FIG. 1. Summary of management strategy for patients with acromegaly. First level, Surgery SR; SRL DR. Second level, SRL SR; monitor SR; increase dose DR. Third level, MRI DR. Fourth level, Radiation DR; Pegvisomant DR. Fifth level, Monitor SR; back to surgery SR. Control is defined by GH and IGF-I measurements as outlined in the text.

used to measure GH) indicate that a random GH below 2.5 ng/ml is associated with a normal life expectancy (11, 14, 78).

Therapeutic decisions should be made according to individualized biochemical and clinical assessment—if IGF-I and GH are elevated, additional therapy should be considered; if IGF-I and GH measurements are discrepant, clinical judgment should be used.

MRI

Postoperative MRI is recommended 3–4 months after surgery to establish a baseline for future follow-up. Similarly, patients receiving medical therapy should be assessed by MRI 3–6 months after starting therapy DR.

The subsequent timing of MRI in patients with acromegaly, after surgery and during medical therapy, depends on disease control. If the patient is surgically “cured,” then MRI may not be necessary (94); however, this is not clearly established and an alternative may be to reduce the frequency of MRI after 2–3 yr of tumor growth control. In patients receiving SRL therapy, if biochemical control is achieved at 1 yr [when most tumor shrinkage will take place (95)], then MRI can be used according to clinical judgment. If disease is not fully controlled with SRL therapy at 1 yr, MRI should be performed 6 months later, then annually. In patients receiving GHRA therapy, MRI should be conducted 6 months after starting therapy, then once per year (because of the potential risk of tumor enlargement).

An important concern with contrast-enhanced MRI is the emerging evidence of associated nephrogenic systemic fibrosis (caused by the gadolinium contrast dye) in certain clinical settings (96). Therefore, renal function should be evaluated before considering the use of gadolinium with MRI.

Pituitary function

After surgery for acromegaly, pituitary function should be measured to assess restoration/preservation of pituitary function

and adrenal insufficiency or posterior pituitary dysfunction (which occurs in a small percentage of patients after transsphenoidal surgery) (18) SR. On the other hand, preoperative hypopituitarism may resolve after surgery. Follow-up assessment should include full pituitary function assessment 3 months after surgery. If this test gives normal results, there is no need for repeat pituitary function tests. However, after radiation therapy, repeated assessment of pituitary function over the years is needed because hypopituitarism can take 10 or more years to develop (69, 97). In patients receiving medical therapy, pituitary function should be assessed as clinically required.

Echocardiography

In patients with no underlying heart disease, echocardiography could be performed at baseline. In the presence of cardiomyopathy, the patient should be referred to a cardiologist for appropriate management.

Sleep disturbance

OSA is a comorbidity of acromegaly that may occur in 25–60% of patients. Sleep quality and disturbances in patients with acromegaly require detailed assessment and appropriate referral for management.

Colonoscopy

At least one baseline colonoscopy assessment is required in all patients with acromegaly. Patients with colonic polyps should be followed according to the international guidelines for colon cancer (98–100) SR.

Summary

Significant progress has been made in the management of acromegaly in recent years. If managed appropriately by a multidisciplinary team with specific experience in managing pituitary tumors, there is no reason for patients to have reduced life expectancy or frequent morbidity. However, unresolved issues exist: the aim of ensuring that patients are managed by appropriately experienced healthcare professional teams is not yet a reality; little is known about the cost-effectiveness of the various management options for acromegaly; and combining treatments may improve patient morbidity and QoL, but more data are needed.

These consensus recommendations are summarized in Fig. 1, but as with most medical management decisions, treatment needs to be individualized and an experienced team should evaluate risks and benefits for each patient. These updated guidelines are aimed to provide clear advice for achieving optimum management and enhancing the health and QoL of all patients with acromegaly.

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Address all correspondence and requests for reprints to: S. Melmed, M.D., Cedars-Sinai Research Institute, 8700 Beverly Boulevard, Room 2015, Los Angeles, California 90048.

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