



UMEÅ UNIVERSITET

Umeå University Medical Dissertations, New Series No 2336

ACROMEGALY

Comorbidities and Novel Diagnostic Tools

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Akademisk avhandling

som med vederbörligt tillstånd av Rektor vid Umeå universitet för avläggande av medicine doktorexamen framläggs till offentligt försvar i Triple Helix, Universitetsledningshuset, fredagen den 24 januari, kl. 9:00.

Avhandlingen kommer att försvaras på engelska.

Fakultetsopponent: Professor Alberto Pereira, Amsterdam University Medical Centers, Amsterdam, Netherlands

Department of Public Health and Clinical Medicine

Organization

Umeå University
Department of Public Health
and Clinical Medicine

Document type

Doctoral thesis

Date of publication

20 December 2024

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Title

Acromegaly: Comorbidities and novel diagnostic tools.

Abstract

Background and aim: Acromegaly is a rare disease caused by a pituitary tumor secreting excess growth hormone, which leads to acral growth, organ enlargement, and facial changes. Patients with acromegaly have an increased risk of type 2 diabetes, cardiovascular disease, and arthropathy. Due to the rarity and slow progression of the disease, there is a considerable diagnostic delay (5–8 years), which contributes to increased morbidity and mortality. This thesis is based on four studies aimed at investigating the presentation of sleep apnea and carpal tunnel syndrome (CTS) in patients with acromegaly and the potential for digital analysis of voice and face to identify patients with acromegaly.

Methods and results: Paper I was a cross-sectional multicenter study of 259 patients with acromegaly: 29% of the patients were previously diagnosed with sleep apnea, with more than half (57%) of these diagnosed prior to the diagnosis of acromegaly. Another 8% of this cohort were found to have undiagnosed sleep apnea by targeted clinical assessment and sleep investigation. Paper II was a retrospective national registry-based study of 556 patients with a diagnosis of acromegaly from the National Patient Registry. It found a 6-fold higher incidence of CTS diagnosis and surgery prior to acromegaly diagnosis compared to the general population. The risk of CTS was higher in women with acromegaly and 84% of patients with CTS were diagnosed and surgically treated before the diagnosis of acromegaly. The potential window of opportunity to diagnose acromegaly earlier led us to investigate new non-invasive screening tools. In Paper III, a multicenter cohort study, we collected voice recordings from 151 patients with acromegaly (23% biochemically active) and 139 matched controls and created a machine learning algorithm, which identified the voice of patients with acromegaly at higher accuracy than experienced endocrinologists (ROC AUC 0.84 vs 0.69). Both biochemically active and controlled patients with acromegaly reported increased voice impairment (Voice Handicap Index) compared to controls. In Paper IV, we used facial images from 155 patients and 153 controls from the same cohort and machine learning algorithms for face analysis to train several machine learning models. The best model matched the accuracy of the compound assessment of 12 experienced endocrinologists (ROC AUC 0.85 vs 0.89) in acromegaly prediction while showing a higher sensitivity (0.82 vs 0.66).

Conclusions: The diagnostic delay in acromegaly leads to the presence of comorbidities long before the disease is recognized. In this time window, non-invasive screening tools based on facial and voice analysis may improve the chances for earlier diagnosis.

Keywords: Acromegaly, diagnostic delay, sleep apnea, carpal tunnel syndrome, face analysis, voice analysis, machine learning

Language

English

ISBN

print:978-91-8070-558-5
PDF: 978-91-8070-559-2

ISSN

0346-6612

Number of pages

109 + 4 papers