



36TH MEETING OF THE

**belgian
endocrine
society**

THURSDAY OCTOBER 15, 2026

FRIDAY OCTOBER 16, 2026

ABSTRACT BOOK

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Program

Thursday October 15, 2026

- 12:30-13:00 **General Assembly**
- 13:00-13:25 **Registration & welcome coffee**
- 13:25-13:30 **Welcome by the president**
- 13:30-14:30 **Rethinking glucagon in T2D and metabolic diseases**
Sponsored symposium by Boehringer Ingelheim
- **Welcome & introduction**
Prof. Dr. Robert Hilbrands (UZ Brussel)
 - **From simple ‘insulin center hormone’ to master regulator of systemic metabolism**
Dr. Amalia Gastaldelli (CNR Pisa, Italy)
 - **Advancing glucagon receptor modulation: the new therapeutic landscape**
Prof. Dr. Roman Vangoitsenhoven (UZ Leuven)
 - **Panel discussion & audience questions**
Prof. Dr. Robert Hilbrands (UZ Brussel)
- 14:30-15:00 **Coffee break**
- 15:00-16:00 **From receptors to reality: GIP signalling and its importance in ectopic fat-driven cardiometabolic disease**
Sponsored symposium by Lilly
- **Welcome & introduction**
Prof. Dr. Nathalie Esser (CHU Liège)
 - **Beyond GLP-1: GIP signalling and its role in multi-agonist incretin efficacy**
Prof. Dr. Timo Müller (Helmholtz Munich, Germany)
 - **From adipocyte biology to the clinic: a deep-dive into ectopic fat-driven disease: OSA**
Prof. Dr. Eveline Dirinck (UZA)
 - **Panel discussion & audience questions**
Prof. Dr. Nathalie Esser (CHU Liège)
- 16:00-16:30 **Coffee break & registration**

- 16:30-17:30 **Attended poster session**
Moderated by Drs. Laura Iconaru & Sarah Vandewalle
- 17:30-18:30 **Regulation of immunity by sex steroid hormones**
Prof. Dr. Marcus Altfeld (University Medical Centre Hamburg, Germany)
Introduced by Prof. Dr. Guy T'Sjoen (UZ Gent)
- 18:30-19:30 **Ketosis-prone diabetes: beyond the traditional classification of diabetes**
Prof. Dr. Laura Orioli (Cliniques Universitaires Saint-Luc Bruxelles)
Introduced by Prof. Dr. Orsalia Alexopoulou (UCL Saint-Luc)
- 19:30-22:00 **Walking dinner**

Friday October 16, 2026

- 08:00-08:30 **Registration**
- 08:30-09:15 **BSED Lecture**
Dr. Manon Lomre (CHU Saint-Pierre, Brussels)
Introduced by Prof. Dr. Laurent Crenier (HUB, Hôpital Erasme)
- 09:15-10:15 **Painful diabetic peripheral neuropathy:
from underdiagnosed complication to optimized patient journey**
Sponsored symposium by Grünenthal
- **Welcome & introduction**
Prof. Dr. Christophe De Block (UZA)
 - **Current concepts in the management of painful diabetic polyneuropathy**
Prof. Dr. Dan Ziegler (German Diabetes Center, Düsseldorf, Germany)
 - **Optimizing the patient journey in Belgium:
a multidisciplinary and case-based approach**
Prof. Dr. Jean-Christophe Philips (CHU Liège)
 - **Panel discussion & audience questions**
Prof. Dr. Christophe De Block (UZA)
- 10:15-10:45 **Coffee break**

10:45-12:15

Communications by young investigators

Sponsored by Ascendis Pharma

Introduced by Prof. Dr. Roman Vangoitsenhoven (UZ Leuven)

Clinical and Translational studies: 4 selected presentations

- **The hidden burden of living with type 1 diabetes: identifying non-medical barriers in adults**
Rani Claerman (UZ Gent)
- **Bone strain index refines 10-year fracture risk stratification across BMD categories in community-dwelling older women: results from the FRISBEE cohort**
Dr. Jeroen de Filette, PhD (CHU Brugman)
- **Endoscopic ultrasound-guided bypass reversal for postprandial reactive hypoglycaemia after Roux-en-Y gastric bypass surgery: Results of a prospective pilot study**
Dr. Emine Gökce (UZ Gent)
- **Validation of an aldosterone-renin ratio-based flowchart for primary aldosteronism screening under interfering antihypertensive medication**
Lisa Kamperdijk (UZA)

Clinical Case Reports: 2 selected presentations

- **Ovarian hyperstimulation syndrome and normal FSH? Maybe not that normal!**
Dr. Astrid Claessens (UZ Leuven)
- **When hyponatremia deceives: isolated hypoaldosteronism as the first sign of autoimmune adrenal insufficiency**
Dr. Anna Vander Heyde (UZ Gent)

12:15-14:00

Lunch at the hotel or guided forest tour with picnic

14:00-14:10

Selected Belgian Publication Award (Diabetes/Metabolism)

Sponsored by Sandoz

Introduced by Prof. Dr. Roman Vangoitsenhoven (UZ Leuven)

- **Recessive TMEM167A variants cause neonatal diabetes, microcephaly and epilepsy syndrome**
Dr. Enrico Virgilio (ULB)

14:10-14:20

Selected Belgian Publication Award (Endocrinology)

Sponsored by the BES

Introduced by Prof. Dr. Orsalia Alexopoulou (UCL Saint-Luc)

- **Diagnostic value of 11C-methionine PET-CT imaging in persistent or recurrent cushing disease after surgery**
Dr. Raluca-Maria Furnica (UCL Saint-Luc)

- 14:20-14:50 **BES Lecture Award**
Sponsored by Novo Nordisk
Introduced by Prof. Dr. Laurent Crenier (HUB, Hôpital Erasme)
- **Iron metabolism of pancreatic β -cells**
Dr. Willem Staels (UZ Brussel)
- 14:50-15:40 **A critical analysis of the new ATA guidelines on differentiated thyroid cancer**
Prof. Dr. Laura Fugazzola (University of Milan, Italy)
Introduced by Prof. Dr. Robert Hilbrands (UZ Brussel)
- 15:40-16:25 **Is there still a role for surgery in the treatment of microprolactinomas?**
Prof. Dr. Peter Kamenicky (Hôpital Bicêtre Paris, France)
Introduced by Prof. Dr. Patrick Petrossians (CHU Liège)
- 16:25-16:30 **Award ceremony of the young investigators**
Moderated by Prof. Dr. Laurent Crenier (HUB, Hôpital Erasme)
- 16:30 **End of meeting**

Abstracts BES 2026

CLINICAL STUDIES	12
Graves' hyperthyroidism following COVID-19 vaccination: a multicenter case series and literature review	13
Prevalence and associated factors of muscle impairment in adults with type 1 diabetes	15
Long-term effectiveness of a reminder system for postpartum glucose intolerance screening in gestational diabetes	16
The hidden burden of living with type 1 diabetes: identifying non-medical barriers in adults	17
Comparison of French and PANOMEN-3 classifications for predicting post-operative evolution in patients with Prolactinoma	19
Evaluation of the efficacy of cabergoline in non-functioning pituitary adenomas: a retrospective clinical study.....	20
Bone strain index refines 10-year fracture risk stratification across BMD categories in community-dwelling older women: results from the FRISBEE cohort	22
Baseline continuous glucose monitoringderived glucometrics in early-stage type 1 diabetes: insights from the EDENT1FI follow-up study	25
Contribution of deep learning to the ultrasound characterization of thyroid nodules: a singlecenter retrospective study	27
Systematic review and meta-analysis of automated insulin delivery systems in pregnancies complicated by type 1 diabetes	29
Endoscopic ultrasound-guided bypass reversal for postprandial reactive hypoglycaemia after Roux-en-Y gastric bypass surgery: results of a prospective pilot study	30
Clinical manifestations and treatment of adults with congenital adrenal hyperplasia: a literature review and application at Ghent University Hospital	32
Validation of an aldosterone-renin ratio-based flowchart for primary aldosteronism screening under interfering antihypertensive medication	34
Kinetics of β -Cell function in cystic fibrosis using HOMA2 indices	36
Low measured free testosterone is associated with worse sexual function in community-dwelling men	37

Current trend in neonatal blood spot TSH suggests normal iodine status of the Flemish population	39
Associations between 25-OH-vitamin D and sexual function outcomes in the European Male Ageing Study (EMAS)	40
Cytokine dynamics following initiation of gender-affirming hormone therapy in transgender subjects	42
Giant pheochromocytomas: clinical presentation and perioperative outcomes	45
Long-term real-world impact of automated insulin delivery on safety, glycemic and parent-reported outcomes in children aged 2 to 6 years with type 1 diabetes	46
The impact of malnutrition on wound healing and clinical outcomes in patients with diabetic foot ulcers	48
Acute and long-term impact on the brain of tight versus liberal blood glucose control in corticosteroid-treated critically ill patients	49
Impact of tight versus liberal blood glucose control in the absence of early parenteral nutrition on neurological injury and two-year outcome in neurointensive care patients	50
Redosing of anti-CD3 antibodies in NOD mice with new-onset diabetes does not alter the effect of a single treatment course	51
CLINICAL CASE REPORTS	58
Beyond thyroid eye disease: remarkable improvement of refractory pretibial myxoedema with teprotumumab	59
Bloom syndrome presenting as early-onset bilateral breast cancer and multisystem metabolic disease: a case report	61
Ovarian hyperstimulation syndrome and normal FSH? Maybe not that normal!	63
Chorioretinal folds in severe Graves' orbitopathy: improvement after teprotumumab	65
The silent catecholamine: a rapidly evolving, exclusively dopamine-secreting pheochromocytoma in a 22-year-old	67
When hyponatremia deceives: isolated hypoaldosteronism as the first sign of autoimmune adrenal insufficiency	69

The abstracts will be published online, as a Volume of Endocrine Abstracts
in html and as a downloadable pdf.

CLINICAL STUDIES

Graves' hyperthyroidism following COVID-19 vaccination: a multicenter case series and literature review

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Dr. Jeroen De Filette - CHU Brugmann

Dr. Lucrezia De Marchi - ZAS CADIX

Dr. David Unuane - VUB - UZ Brussel

Dr. Corina Andreescu - VUB - UZ Brussel

Dr. Kris Poppe - CHU Saint-Pierre

Dr. Laura Iconaru - CHU Brugmann

Dr. Evelyne Maillart - CHU Brugmann

Dr. Dragos Barglazan - CHU Brugmann

Abstract

Objectives

Since the introduction of COVID-19 vaccination, cases of Graves' disease (GD) occurring shortly after immunization have been reported. The objective of this study was to describe and compare the clinical, biochemical and imaging features of GD diagnosed after vaccination with those of other newly diagnosed GD cases.

Methods

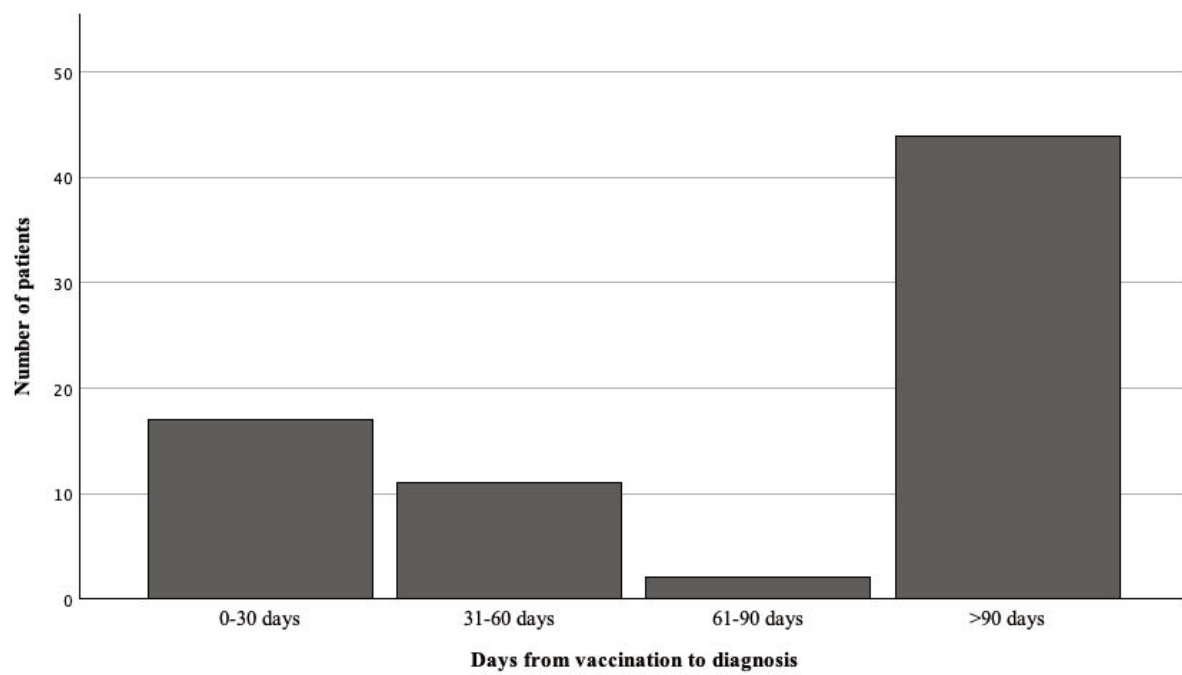
A multicenter retrospective case series was conducted in three university hospitals in Brussels, Belgium. Adults diagnosed with de novo GD between 1 January 2021 and 31 October 2022 were included. Patients were categorized into three groups according to vaccination status and timing of disease onset: early-onset GD (≤ 30 days) after COVID-19 vaccination, later-onset GD (> 30 days), and GD in unvaccinated individuals. In addition, a literature review of peer-reviewed case reports and case series of de novo GD following COVID-19 vaccination was performed.

Results

A total of 160 patients were included: 17 with early-onset post-vaccination GD, 57 with later-onset disease, and 86 unvaccinated at diagnosis of GD. No significant differences were observed between the three groups with respect to clinical, biochemical, thyroid ultrasound or initial treatment characteristics. Age differed significantly between groups, with patients in the early-onset group being younger ($p = 0.002$). All other assessed parameters were comparable.

Conclusion

In this multicenter retrospective series, GD diagnosed after COVID-19 vaccination did not demonstrate a distinct clinical, biochemical or imaging phenotype compared with GD in unvaccinated individuals. These results support the use of standard diagnostic and therapeutic strategies for GD, irrespective of COVID-19 vaccination status or timing.



Prevalence and associated factors of muscle impairment in adults with type 1 diabetes

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Prof. Vanessa Preumont - UCLouvain - Cliniques universitaires Saint-Luc

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Abstract

Aims

Sarcopenic obesity (SO) is an emerging comorbidity in adults with type 1 diabetes (T1D) (1,2). This study aimed to assess the prevalence of SO and muscle impairment, and to identify associated factors in adults with T1D.

Methods

We conducted a single-center prospective observational study at a tertiary care center including adults with T1D aged ≥ 18 years receiving insulin therapy for at least one year. Overweight and obesity were defined according to body mass index (BMI). Physical activity was assessed using the Godin–Shephard Leisure-Time Physical Activity Questionnaire (GLTEQ). Body composition was assessed by bioelectrical impedance analysis, with skeletal muscle mass (SMM) estimated using the Janssen equation. Handgrip strength (HGS) was used to assess muscle function. SO was defined according to the ESPEN/EASO consensus as the coexistence of excess adiposity (elevated fat mass/body weight), dynapenia (low HGS), and myopenia (low SMM/body weight) (1). Multivariable logistic regression adjusted for age and sex was used to identify factors associated with muscle impairment (dynapenia and/or myopenia with or without excess adiposity).

Results

Fifty-seven adults with T1D (median age 49 years; 44% women; median diabetes duration 22 years; median HbA1c 7.2%) have been enrolled to date. According to BMI, 40% of participants were overweight and 30% were obese. SMM and HGS were significantly higher in men than in women, as expected. Although no participant met the criteria for SO, excess adiposity, myopenia and dynapenia were present in 25%, 18% and 4% of participants, respectively. Overall, 21% exhibited muscle impairment (dynapenia and/or myopenia). Higher total daily insulin dose was independently associated with muscle impairment (adjusted OR 1.026, 95% CI 1.001– 1.052; $p=0.038$). No significant associations were observed for age, diabetes duration, HbA1c or physical activity.

Conclusions

Although no cases of SO were identified in this preliminary cohort, one in five adults with T1D exhibited muscle impairment, supporting routine assessment of muscle health in adults with T1D. Ongoing longitudinal follow-up will determine whether these muscle alterations predict progression to overt SO.

References

1. Donini LM, Busetto L, Bischoff SC, Cederholm T, Ballesteros-Pomar MD, Batsis JA et al. Definition and Diagnostic Criteria for Sarcopenic Obesity: ESPEN and EASO Consensus Statement. *Obes Facts*. 2022;15(3):321-335. doi: 10.1159/000521241.
2. Andreo-López MC, Zarco-Martín MT, Contreras-Bolívar V, Fernández-Soto ML. Prevalence of Sarcopenia and Dynapenia and Related Clinical Outcomes in Patients with Type 1 Diabetes Mellitus. *Nutrients*. 2023 Nov 24;15(23):4914. doi: 10.3390/nu15234914.

Long-term effectiveness of a reminder system for postpartum glucose intolerance screening in gestational diabetes

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Abstract

Background and aims

Women with a history of gestational diabetes (GDM) have an increased risk of developing type 2 diabetes later in life. We evaluated the long-term feasibility and effectiveness of a regionally implemented GDM recall register to stimulate postpartum screening and assess (pre)diabetes prevalence up to 10 years postpartum.

Methods

We evaluated the “Sweet Pregnancy” GDM recall register, implemented in the northern part of Belgium, from 2009 to 2025. Women with a history of GDM received annual reminders for screening with a fast-ing plasma glucose in primary care. Response rates, self-reported screening uptake, and cumulative incidence of (pre)diabetes were analyzed.

Results

27,173 women were registered with a mean follow-up of 4.4 years. The yearly response rates (among both responders and non-responders combined) varied from 48.4% (11,048) after the first year to 34.2% (4,116) after the fifth year, and 27.6% (1,190) after 10 years. Among responders, during the follow-up period of 3 and 5 years, 80.4% and 81.9% received at least one screening test, respectively. Non-responders were more often under 30 years of age (45.4% vs. 42.0%, $p < 0.001$) and obese (32.6% vs. 24.8%, $p < 0.001$) compared to responders. After 10 years, the cumulative incidence of diabetes was 11.0% and of impaired fasting glucose 34.7%.

Conclusion

This large-scale register implemented in normal routine, up to 10 years of follow-up, indicates a feasible and effective reminder system to stimulate postpartum diabetes screening in women with prior GDM. The high cumulative incidence of (pre)diabetes underscores the importance of long-term follow-up and targeted interventions to prevent progression to type 2 diabetes in this high-risk population.

The hidden burden of living with type 1 diabetes: identifying non-medical barriers in adults

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Abstract

Background and aims

Adults with type 1 diabetes mellitus are faced every day with a challenging disease management. In addition to therapeutic aspects such as achieving stable glycaemic control, social, emotional and practical barriers play an important role. Non-medical barriers in adults living with type 1 diabetes remain under-explored, despite the impact on quality of life and diabetes management. Therefore, this qualitative study aims to identify nonmedical barriers in adults living with type 1 diabetes. Methodology: A qualitative research design was used, consisting of 32 semistructured interviews and 8 focus groups with 60 adults living with type 1 diabetes. Inclusion criteria were a minimum diabetes duration of 2 years and Dutch-speaking proficiency. The focus group discussions and interviews were audio recorded and transcribed verbatim. The data were analysed thematically through an iterative coding process guided by the socio-ecological model¹. Additionally, participants completed the Audit of Diabetes Dependent Quality of Life (ADDQoL) questionnaire² to explore the impact of type 1 diabetes on quality of life.

Results

The study population (n=60) consisted of 65% women (n=39) and 35% men (n=21), with a mean age of 48.6 years (SD=20.3; range 18–83) and a mean diabetes duration of 29.4 years (SD=16.4; range 2–65). Just over half of participants used insulin pump therapy (55%, n=33), while the remainder used multiple daily injections (45%, n=27). Educational attainment was distributed across secondary school (25%, n=15) and higher education (75%, n=45). Analysis yielded 769 coded fragments representing non-medical barriers, which clustered into eight main themes: (1) diabetes distress and psychological burden, (2) practical life domains (work, diet, exercise, sleep, mobility, travel), (3) social life, intimacy and stigma, (4) family life and planning, (5) work and education, (6) healthcare system and provider relationships, (7) diabetes technology, and (8) financial barriers. Most codes clustered in themes related to work and education and sports and physical exercise within daily life, alongside prominent codes on lack of understanding in the social/work environment and diabetes distress, indicating these as dominant barriers across adulthood. ADDQoL results showed that all domains were negatively affected by diabetes, with the greatest negative impact reported for freedom to eat, physical capabilities, and feelings about the future.

Conclusion

Alongside the medical burden of type 1 diabetes, adults experience substantial non medical barriers that markedly affect their emotional well being and social participation. These non-medical barriers notably shape the lived experience of adults with type 1 diabetes, with the continuous daily burden of managing the condition contributing prominently to psychological and social barriers. As reflected in the ADDQOL findings, these barriers have a negative impact on quality of life, highlighting the need for greater attention to psychosocial and structural factors that are often overlooked in healthcare.

References

1. McLeroy KR, Bibeau D, Steckler A, Glanz K. An ecological perspective on health promotion programs. *Health Educ Q.* 1988;15(4):351–377. doi:10.1177/109019818801500401.
2. Bradley C, Todd C, Gorton T, Symonds E, Martin A, Plowright R. The development of an individualized questionnaire measure of perceived impact of diabetes on quality of life: the ADDQoL. *Qual Life Res.* 1999;8(1–2):79–91. doi:10.1023/A:1026485130100.

Comparison of French and PANOMEN-3 classifications for predicting post-operative evolution in patients with prolactinoma

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Abstract

Background

The French five-tiered classification assesses recurrence/progression risk in pituitary tumors (1), but data on prolactinomas is scarce. Clinical validation of the new PANOMEN-3 classification is also needed (2). We compared both classifications in predicting post-operative evolution in patients with prolactinoma.

Methods

We retrospectively analyzed patients operated for prolactinoma (2006–2024) with confirmed histology and ≥ 12 months follow-up. Recurrence was defined as new prolactin increase >3 months post-curative surgery. Progression was defined as $>20\%$ increase in residual tumor diameter. We defined disease free status at last visit as a normal prolactin without dopamine agonist treatment.

Results

71 patients (44 women, 27 men) were included. 35 were initially cured by surgery; 7/35 (20%) recurred (after a median of 18 months). 36 patients were not cured by surgery; 12/36 (33%) progressed (after a median of 12 months; 11/12 within 4 years). Progression/recurrence (27%) was significantly associated with French proliferative nature ($p=0.003$) but not invasiveness ($p=0.734$). The overall French grade was associated with progression ($p=0.027$) but not recurrence ($p=0.201$). PANOMEN-3 grade was associated with neither recurrence ($p=0.528$) nor progression ($p=0.440$). Disease free status at last visit was significantly associated with both the French (58%, 66%, 0% and 0% for grades 1a, 1b, 2a and 2b respectively, $p<0.001$) and PANOMEN-3 grades (86%, 58%, 14% and 0% for grades 0, 1, 2 and 3 respectively, $p<0.001$).

Conclusion

The proliferative nature of the tumor, as defined by the French classification, was the most important predictor of progression/recurrence, highlighting the need for careful follow-up of these patients, especially during the first 4 years after surgery. For disease free status at last visit, PANOMEN-3 grade might provide better discriminatory power because of the linear decrement in prognosis across grades.

References

1. Trouillas J, Roy P, Sturm N et al, A new prognostic clinicopathological classification of pituitary adenomas: a multicentric case-control study of 410 patients with 8 years post-operative follow-up. *Acta Neuropathol.* 2013 Jul;126(1):123-35. doi: 10.1007/s00401-013-1084-y.
2. Ho KKY, Flesteriu M, Wass J, et al. A proposed clinical classification for pituitary neoplasms to guide therapy and prognosis. *Lancet Diabetes Endocrinol.* 2024;12(3):209-214. doi:10.1016/S0140-6736(07)61602-X

Evaluation of the efficacy of cabergoline in non-functioning pituitary adenomas: a retrospective clinical study

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Abstract

Introduction

Non-functioning pituitary adenomas (NFPAs) are benign sellar tumors characterized by the absence of clinical and biochemical evidence of hormonal hypersecretion. Their management relies on several therapeutic strategies, including active surveillance, surgery, radiotherapy, and medical treatment with cabergoline (CBG). However, the efficacy of CBG remains controversial, and its use is not currently supported by a clear consensus. The aim of this study was to evaluate the efficacy of CBG in inducing tumor shrinkage or stabilization in patients with NFPAs.

Methods

We conducted a single-center retrospective clinical study (CHU de Liège), including 234 patients with NFPAs (146 treated with CBG and 88 untreated). The cohort comprised untreated adenomas, postoperative remnants, and recurrent tumors. Data were collected from an internal endocrinology registry of patients managed for intrasellar disorders and supplemented by extraction from the electronic medical records. The primary endpoint was tumor shrinkage under CBG treatment, while the secondary endpoint was tumor stabilization.

Results

Tumor shrinkage was observed in 11.64% of treated patients compared with 5.68% in the untreated group. Complete tumor disappearance occurred in four cases (baseline tumor sizes: 8, 7, 11, and 18 mm), while the median reduction among the remaining responders was 5 mm. Tumor progression was observed in 19.86% of treated patients versus 48.86% of controls, whereas tumor stabilization was achieved in 68.49% and 45.45% of patients, respectively. These differences were statistically significant ($p < 0.001$).

Conclusion

In our study, CBG was associated with a more limited effect on tumor shrinkage than that reported in the current literature. The observed rate of tumor stabilization is likely overestimated due to several confounding factors, including relatively short follow-up periods and limited treatment duration in some patients. Although tumor progression was less frequent in the treated group, this finding should be interpreted cautiously given the shorter median follow-up in these patients (4.5 years vs. 10.5 years). Prospective randomized controlled studies are needed to better define the role of cabergoline in the management of NFPAs.

Groupe		Evolution			Total
		Tumor progression	Tumor shrinkage	Tumor stabilization	
Treated group	Count	29.00	17.00	100.0	146.0
	% within row	19.86 %	11.64 %	68.49 %	100.00 %
Untreated group	Count	43.00	5.000	40.00	88.00
	% within row	48.86 %	5.68 %	45.45 %	100.00 %
Total	Count	72.00	22.00	140.0	234.0
	% within row	30.77 %	9.40 %	59.83 %	100.00 %

Chi-Squared Tests

	Value	df	p
X ²	21.95	2	< .001
N	234		

Note. Continuity correction is available only for 2x2 tables.

Figure 1. Contingency Table

References

1. Iglesias P, Biagetti B, Araujo-Castro M, et al. Effect of cabergoline on tumor remnant after surgery in nonfunctioning pituitary adenoma. *J Neurooncol.* 2022 Nov;160(2):351-359.
2. Batista RL, Musolino NRC, Cescato VAS, et al. Cabergoline in the management of residual nonfunctioning pituitary adenoma: a single-center, open-label, 2-year randomized clinical trial. *Am J Clin Oncol.* 2019 Feb;42(2):221-227.
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Bone strain index refines 10-year fracture risk stratification across BMD categories in community-dwelling older women: results from the FRISBEE cohort

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Abstract

Introduction

Most fragility fractures occur in women without densitometric criterion for osteoporosis, highlighting the limitation of bone mineral density (BMD) measurement alone. This study evaluated whether total hip Bone Strain Index (BSI), a DXA-based finite element analysis index, provides fracture risk information beyond WHO-defined BMD categories. It also explored implications for treatment allocation and number needed to treat (NNT).

Methods

We analyzed 3,338 community-dwelling older women from the FRISBEE cohort with 10-year follow-up. Total hip BSI was calculated from baseline DXA scans. Associations between BSI and incident fragility fractures were assessed within BMD categories using Cox models, adjusted for age, total hip BMD, or FRAX®. Exploratory analyses estimated preventable fractures and NNT assuming a 30% fracture risk reduction.

Results

803 women (24.1%) sustained at least one fragility fracture. Per 1-SD increase, total hip BSI was associated with fracture risk in normal BMD (HR 1.36, 95% CI 1.19–1.55), osteopenia (HR 1.24, 95% CI 1.14–1.35), and osteoporosis (HR 1.25, 95% CI 1.09–1.43). BSI remained independently associated with fracture risk after adjustment for age and total hip BMD (HR 1.15, 95% CI 1.06–1.25; $p = 0.001$) or FRAX® (HR 1.19, 95% CI 1.11–1.28; $p < 0.001$). Compared with densitometric osteoporosis, adding elevated BSI in women with osteopenia increased estimated preventable fractures from 51 to 107, with NNT increasing from 8.7 to 9.3.

Conclusions

Total hip BSI was independently associated with fragility fractures across WHO-defined BMD categories. BSI provided information beyond BMD and FRAX® and could support individualized risk evaluation and treatment allocation.

Table 1. Hazard ratio for all fractures at 10 years, obtained by univariate Cox regression

Variable	HR	95% CI	p-value
Separate models by sub-groups			
Normal BMD* sub-group			
Total hip BSI (+ 1 SD)	1.36	1.19 - 1.55	< 0.001
Osteopenia* sub-group			
Total hip BSI (+ 1 SD)	1.24	1.14 - 1.35	< 0.001
Osteoporosis* sub-group			
Total hip BSI (+ 1 SD)	1.25	1.09 - 1.43	0.001
Stratified (pooled) model (strata = Osteoporotic status)			
Total hip BSI (+ 1 SD)	1.28	1.19 - 1.36	< 0.001

Figure 1. *Osteoporotic status as defined by the World Health Organization, based on BMD: osteoporosis is a T-score ≤ -2.5 or more, i.e. 2.5 standard deviations below the average for young healthy adults Osteopenia is a T-score between -1.0 and -2.5. BMD is considered normal otherwise. Abbreviations: BMD: Bone Mineral Density; BSI: Bone Strain Index; CI: Confidence interval; HR: Hazard ratio; SD: Standard deviation.

Table 2. Adjusted hazard ratio for risk of fracture obtained by multiple Cox regression, stratified by osteoporotic status*

Model 1 (Age + Total hip BMD)			
Variable	HR	95% CI	p-value
Total hip BSI (+ 1 SD)	1.15	1.06 - 1.25	0.001
Model 2 (FRAX®)			
Variable	HR	95% CI	p-value
Total hip BSI (+ 1 SD)	1.19	1.11 - 1.28	< 0.001

Figure 2. *Osteoporotic status as defined by the World Health Organization, based on BMD: osteoporosis is a T-score ≤ -2.5 or more, i.e. 2.5 standard deviations below the average for young healthy adults Osteopenia is a T-score between -1.0 and -2.5. BMD is considered normal otherwise. Abbreviations: BMD: Bone mineral density; BSI: Bone strain index; CI: Confidence interval; HR: Hazard ratio, SD: Standard deviation.

Table 3. Number needed to treat (NNT) according to treatment attribution criteria

Treatment attribution criteria	Treated patients	Fractures	Preventable fractures (30%)	NNT
No criteria (treat all)	3221	774	232	13.9
BMD-based osteoporosis	444	171	51	8.7
BMD-based osteoporosis or FRAX >20%	551	214	64	8.6
BMD-based osteoporosis or BMD-based osteopenia & BSI ≥ 1.69	998	357	107	9.3

Figure 3. Osteoporotic status as defined by the World Health Organization, based on BMD: osteoporosis is a T-score ≤ -2.5 or more, i.e. 2.5 standard deviations below the average for young healthy adults. Osteopenia is a T-score between -1.0 and -2.5.

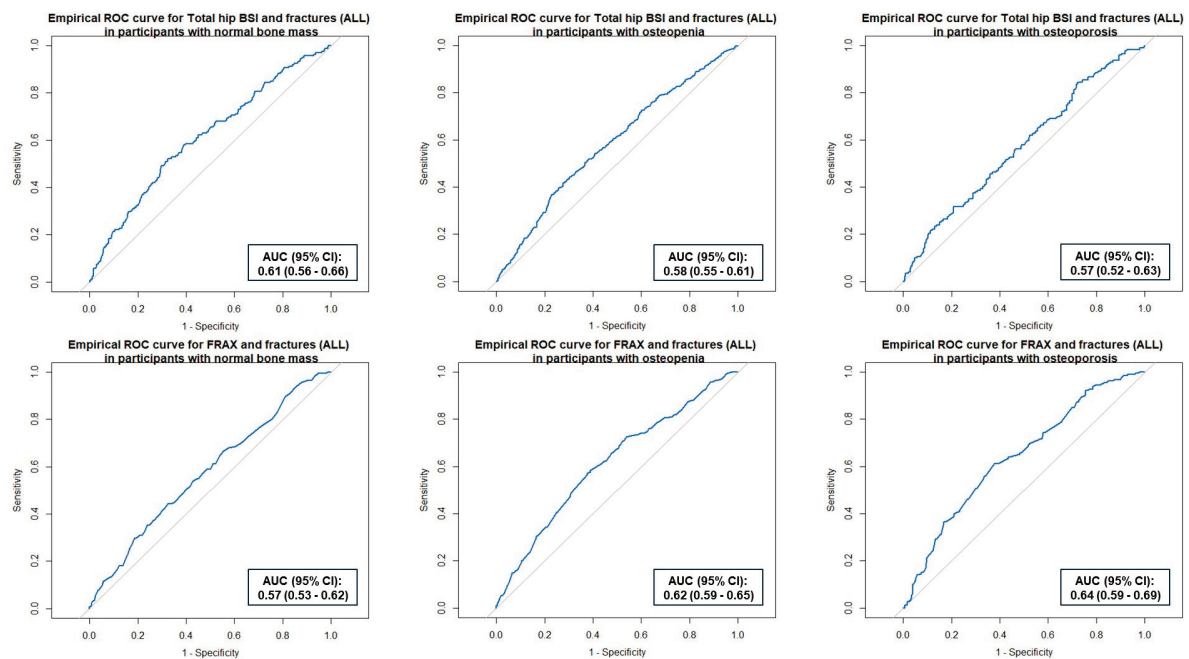


Figure 4. Empirical Receiver Operating Characteristics (ROC) curves for Total hip BSI and FRAX, and all fractures.

Baseline continuous glucose monitoring-derived glucometrics in early-stage type 1 diabetes: Insights from the EDENT1FI follow-up study

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Abstract

Background and aims

To assess baseline continuous glucose monitoring (CGM) derived time >140 mg/dL ($T>140$) in children with early-stage type 1 diabetes (T1D) enrolled in the EDENT1FI follow-up study. Materials and Methods: Baseline was defined as the first study visit after confirmed presence of ≥ 2 islet autoantibodies (IAbs). T1D stage was determined using oral glucose tolerance test results and HbA1c. A progression likelihood score was calculated to estimate the individual risk of progression to stage 3 T1D. All participants received a CGM device. Based on T1D stage and risk tier, participants were categorized into four groups: group 1 (T1D stage 1, tier 1), group 2 (T1D stage 1, tier 2), group 3 (T1D stage 1, tier 3), group 4 (T1D stage 2). Data were reported as mean ($\pm$ SD) or n (%).

Results

Of 124 children with ≥ 2 IAbs, mean age was 9.4 (± 3.7) years and 54.8% were girls. Twenty-six (21.0%), 63 (50.8%), 19 (15.3%), and 16 (12.9%) children were classified in group 1, 2, 3, and 4, respectively. Mean $T>140$ was 1.3% (± 1.4), 2.6% (± 3.7), 2.3% (± 2.1), and 5.5% (± 6.8) in participants of group 1, 2, 3, and 4, respectively. Substantial overlap in individual $T>140$ was observed between groups, with marked day-to-day variability in individuals within the same group (Figure 1).

Conclusion

In children with early-stage T1D, baseline CGM-derived $T>140$ showed substantial inter- and intra-individual overlap, limiting discrimination. Longitudinal CGM evaluation and advanced analytics may help identify glycemic patterns associated with disease stage and improve prediction of progression toward more advanced T1D stages. EDENT1FI is funded by IHI JU grant No 101132379.

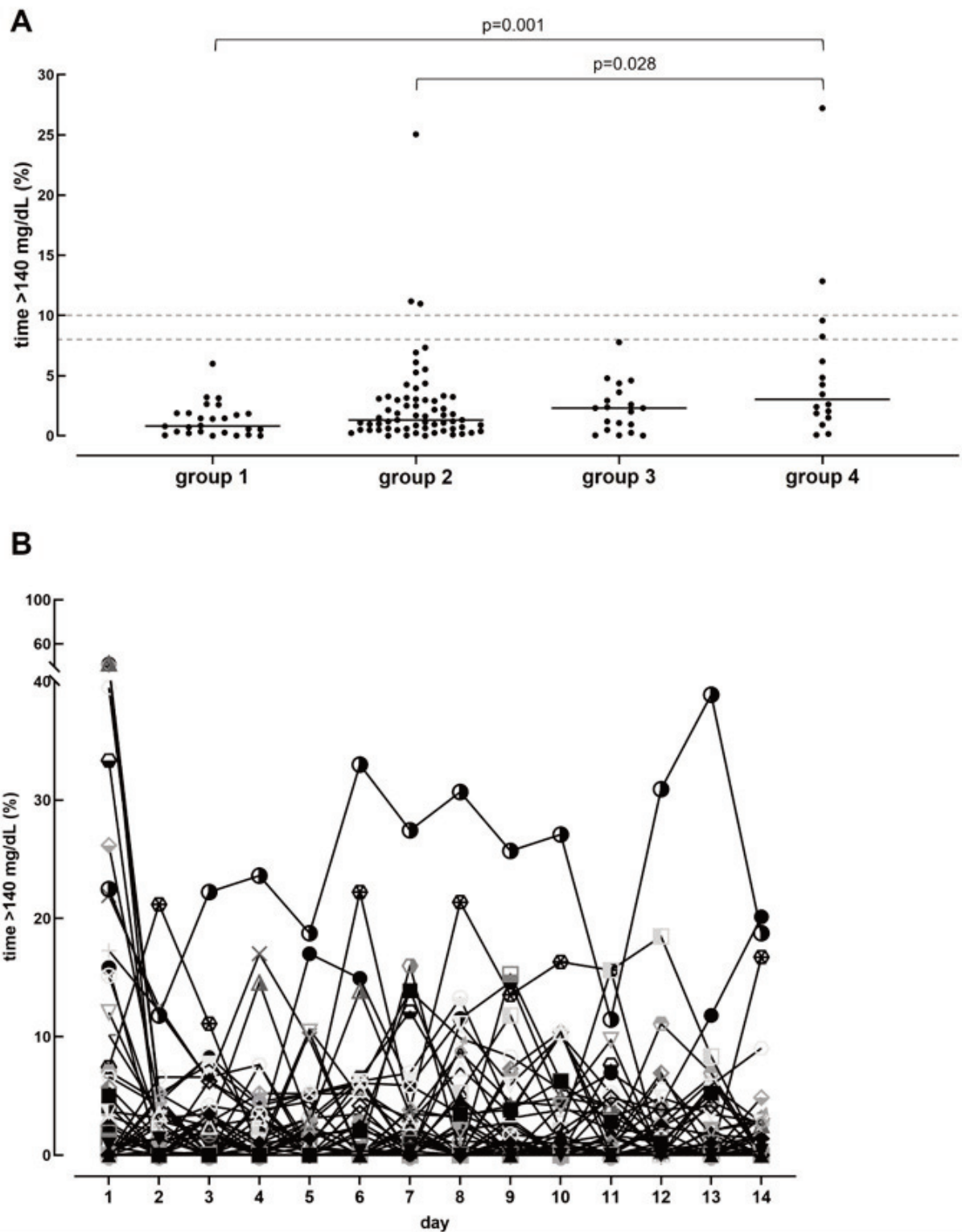


Figure 1. Distribution of individual mean time >140 mg/dL ($T>140$). Data points represent the mean $T>140$ over 24 hours: (A) for all individuals, grouped by disease stage and risk tier; (B) for participants in group 2 only, with each line representing day-to-day variability within a single participant. Groups are defined by disease stage and risk tier. P-values are based on Kruskal-Wallis test with post-hoc pairwise comparisons; only significant comparisons are shown.

Contribution of deep learning to the ultrasound characterization of thyroid nodules: a single-center retrospective study

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Abstract

Introduction

The ultrasound prevalence of thyroid nodules has increased significantly over recent decades and currently exceeds 60%, primarily due to advances in imaging techniques. This increased detection of nodules in asymptomatic patients poses a major clinical challenge: accurately distinguishing benign from malignant lesions while avoiding unnecessary investigations and surgeries.

Thyroid ultrasound remains the first-line imaging modality for malignancy risk assessment; however, it has limited specificity and substantial interobserver variability. To address these limitations, the scientific community is exploring other approaches to improve malignancy risk stratification, particularly deep learning techniques, which hold considerable promise in medical image analysis.

Design and methods

We conducted a single-center retrospective study to evaluate the performance of a deep learning model for the ultrasound differentiation of benign and malignant thyroid nodules. This study represents a preliminary phase and included 8 benign and 6 malignant nodules, all with definitive histopathological diagnosis. As these nodules were recorded on video, we applied data augmentation techniques to increase the number of images available for training. In total, we obtained 2,569 images from these 14 nodules, of which 386 were reserved for the validation phase. Dedicated software was developed in Python using the PyCharm integrated development environment. Successive training cycles of supervised learning were performed to progressively improve the model's performance. We compared two deep learning approaches: a model trained from scratch and a model pretrained on a general radiological image dataset.

Results

The deep learning model without pretraining demonstrated, after 6 training cycles, an AUC of 0.666, a precision for benign nodule detection of 0.593, and a precision for malignant nodule detection of 0.000. After 24 training cycles, this model yielded similar results. The pretrained deep learning model achieved, after 6 training cycles, an AUC of 0.934, a precision for benign nodule detection of 0.911, and a precision for malignant nodule detection of 0.846. After 24 training cycles, this model reached an AUC of 0.951, a precision for benign nodule detection of 0.927, and a precision for malignant nodule detection of 0.849. The sensitivity of the pretrained model was 0.873 after 6 training cycles and 0.898 after 24 training cycles, while specificity was 0.891 after both 6 and 24 training cycles.

Conclusion

Artificial intelligence represents a significant advancement in thyroid nodule evaluation, offering promising diagnostic performance and the potential to improve the selection of nodules eligible for fine-needle aspiration biopsy. However, its integration into clinical practice remains limited by the lack of prospective validation and standardization. Our study, involving a deep learning model developed and validated at the University Hospital of Liège, reveals encouraging results for the pretrained deep learning model. These findings should nonetheless be interpreted in light of methodological limitations, particularly the very limited number of nodules included.

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Systematic review and meta-analysis of automated insulin delivery systems in pregnancies complicated by type 1 diabetes

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Abstract

Objective

Pregnancies complicated by type 1 diabetes are associated with a high risk of adverse pregnancy outcomes. Randomized controlled trials (RCT's) with automated insulin delivery (AID) were not powered to detect differences in pregnancy outcomes. Therefore, we performed a systematic review and meta-analysis to assess the impact of AID use on pregnancy outcomes.

Research design and methods

A systematic search was performed in accordance with PRISMA 2020 guidelines. PubMed, Embase, Web of Science, Scopus, Cochrane, CINAHL, ClinicalTrials.gov and ICTRP were searched up to 17 March 2026. RCT's investigating the use of AID systems in pregnancies complicated by type 1 diabetes were included. Primary outcomes included hypertensive disorders, LGA, birthweight, neonatal hypoglycemia requiring treatment, NICU admission, preterm birth, and neonatal death. Two reviewers independently screened studies, extracted data, and assessed risk of bias using the Cochrane Risk of Bias tool.

Results

Of the 1,310 identified studies, 849 remained after deduplication. Four RCTs, including 333 women with type 1 diabetes, met the inclusion criteria. Although AID did not significantly improve the primary pregnancy outcomes, it significantly improved maternal glycemia, including overnight time in range, overnight time above range, time below range, glycemic variability, and gestational weight gain. Restricting the analysis to the AiDAPT and CIRCUIT trials showed a significant reduction in preeclampsia with AID.

Conclusions

AID improves several maternal glycemic outcomes and reduces gestational weight gain. Only AID systems that achieved significantly higher time in range demonstrated a reduction in preeclampsia.

Endoscopic ultrasound-guided bypass reversal for postprandial reactive hypoglycaemia after Roux-en-Y gastric bypass surgery: results of a prospective pilot study

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Abstract

Background And Aim

Postprandial reactive hypoglycaemia syndrome (PRHS) is an increasingly recognized complication after Roux-en-Y gastric bypass (RYGB) surgery. Surgical reversal is considered in severe, therapy-refractory cases but may still fail and often leads to significant weight regain. We investigated whether endoscopic ultrasound (EUS)guided bypass reversal could be a minimally invasive alternative to surgery in this patient population.

Methods

We conducted a prospective clinical study in 12 RYGB patients with severe, therapyrefractory PRHS. Patients underwent EUS-assisted placement of a 20 × 10 mm lumenapposing metal stent (LAMS) between the gastric pouch and the excluded stomach. Patients were followed prospectively for 6 months with 4 study visits, including clinical and laboratory assessment, and a mixed-meal test at 6 months. The primary outcome measures of interest were clinical response (immediate and sustained) and adverse event rate. Other outcome measures included technical success, procedure duration, quality of life and weight change. Technical success was defined as successful LAMS placement. Clinical success was defined as a patient-reported clinically meaningful improvement of symptoms. The AGREE classification was used to grade adverse events. Quality of life was reported on a visual analogue scale (VAS).

Results

Twelve patients (92% women) with a mean age of 58 years [range 34–65] and a mean BMI of 25 kg/m² [range 18–34] underwent the procedure. Technical success was achieved in all patients, with a mean procedural duration of 18 minutes [range 10– 38]. Immediate clinical success was achieved in 10/12 (83.3%) patients, accompanied by a significant improvement in quality of life compared to baseline (VAS 3.0 to 8.0, increase 5.5 points [97.85% CI 0.0–8.0], $p = 0.0078$). Two responders prematurely ended the study. Maintenance of response was achieved in 7/8 (87.5%) remaining patients (VAS increase 6.0 points [99.22% CI 2.0–8.0], $p = 0.0078$). Adverse events occurred in 2/10 patients and were classified as moderate. One patient had gastric discomfort and reflux symptoms controlled by medical treatment. The other patient had a stent migration resulting in loss of response. Restoration of clinical response was seen after endoscopic repositioning and fixation of the stent. Mean weight change was -0.3 kg (95% CI -3.886–3.286; $p = 0.8541$).

Conclusion

In this prospective pilot study, EUS-guided gastric bypass reversal appeared to be an effective and safe minimally invasive alternative to surgical reversal in RYGB patients with severely invalidating PRHS.

EUS-guided Gastric Bypass Reversal for Postprandial Reactive Hypoglycaemia (PRHS)

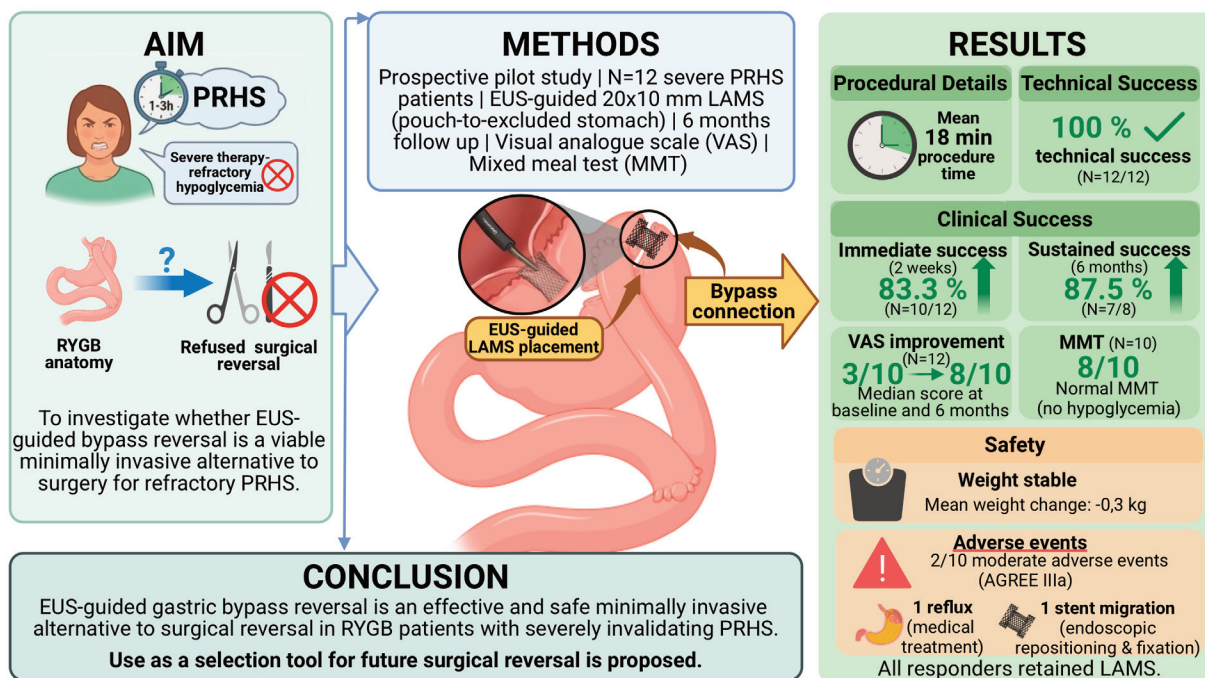


Figure 1. Graphical abstract

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Clinical manifestations and treatment of adults with congenital adrenal hyperplasia: a literature review and application at Ghent University Hospital

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Abstract

Introduction / research aim

Congenital adrenal hyperplasia (CAH) encompasses a group of autosomal recessive disorders resulting from inadequate cortisol production, mainly caused by 21-hydroxylase deficiency. Classic CAH is the most common cause of atypical external genitalia in 46,XX neonates and primary adrenal insufficiency in childhood. Nonclassic CAH is more common, presenting in patients with signs of hyperandrogenism or subfertility. The management of CAH is lifelong and entails various long-term disease- and treatment-related complications. This master's thesis describes the adult patients with CAH followed at Ghent University Hospital and evaluates our management approach against current treatment guidelines.

Methods

A literature review was conducted using Medline, Google Scholar, Embase and Cochrane Library databases. A retrospective study was performed involving data extraction from electronic patient records. Inclusion criteria were adults (≥ 18 years) diagnosed with CAH who had attended the Department of Endocrinology within the past two years.

Results

Our adult CAH patient population consists of 53 patients: 24 with salt-wasting classic CAH (45.3%), 6 with simple-virilizing classic CAH (11.3%), 7 with unclassified classic CAH (13.2%), and 16 with nonclassic CAH (30.2%). Most patients harbor a CYP21A2 mutation (92.5%), although some patients carry mutations in CYP11B1, CYP17A1 and StAR. Patient data regarding diagnostic work-up, treatment, fertility/pregnancy and monitoring are presented and compared with the recommendations of current treatment guidelines.

Conclusion

The general approach at Ghent University Hospital aligns well with current guidelines. CAH is a rare, complex condition requiring a holistic approach within specialized centers. Multicenter data collection, involving the exchange of experience, knowledge, and ideas among healthcare providers and patients with CAH, remains a priority and contributes to the optimization of clinical practice. Key words: congenital adrenal hyperplasia, CAH, 21-hydroxylase deficiency, CYP21A2, adrenogenital syndrome, diagnosis/ diagnostics, treatment/therapy, management, monitoring, guidelines

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Validation of an aldosterone-renin ratio-based flowchart for primary aldosteronism screening under interfering antihypertensive medication

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Abstract

Background

Primary aldosteronism (PA) is a common cause of secondary hypertension but remains substantially underdiagnosed. To increase screening rates, several strategies have been proposed, including screening without withdrawal of interfering antihypertensive medication. In 2022, Mulatero et al. published a flowchart and in 2025 the Endocrine Society (ES) incorporated one into its guidelines, both enabling PA screening without withdrawal of possible interfering antihypertensive medication (1,2). However, neither flowchart has undergone external validation. Therefore, the present study aimed to validate both flowcharts in an independent cohort.

Methods

This retrospective single-center study included 77 adult patients referred to the endocrinology outpatient clinic of the University Hospital Antwerp for screening of secondary hypertension between January 2022 and May 2026. All patients underwent PA screening without withdrawal of possible interfering antihypertensive medication and again after drug adjustment. A positive standard screening result was defined as plasma aldosterone concentration ≥ 100 pg/mL, direct renin concentration < 8.2 μ U/mL, and aldosterone-renin ratio ≥ 25 (pg/mL)/(μ U/mL) after drug adjustment. The diagnostic performance of both flowcharts was evaluated against the outcome of standard PA screening.

Results

The cohort comprised 77 patients (57.1% female; median age 48 years). Patients were treated with a mean of 2.42 antihypertensive drug classes and a median cumulative defined daily dose equivalent of 2.50. At screening, 10.4% of patients were receiving mineralocorticoid receptor antagonists. Using standard screening criteria, 33.8% of the cohort screened positive for PA. The Mulatero flowchart could not be applied in 41.6% of patients due to the use of incompatible combinations of antihypertensive medications. In the remaining cohort ($n = 45$), the flowchart yielded a definitive screening outcome (positive/negative) in 60.0%, with an overall concordance of 85.2% compared with standard PA screening. Among 19 patients classified as negative by the Mulatero flowchart, two were positive on standard screening, indicating potential missed PA cases. The ES flowchart provided a definitive classification in 12 patients (15.6%), with 91.7% concordance with standard screening. All patients classified as negative by the ES flowchart were also negative according to standard screening.

Conclusion

The cohort comprised 77 patients (57.1% female; median age 48 years). Patients were treated with a mean of 2.42 antihypertensive drug classes and a median cumulative defined daily dose equivalent of 2.50. At screening, 10.4% of patients were receiving mineralocorticoid receptor antagonists. Using standard screening criteria, 33.8% of the cohort screened positive for PA. The Mulatero flowchart could not be applied in 41.6% of patients due to the use of incompatible combinations of antihypertensive medications. In the remaining cohort (n = 45), the flowchart yielded a definitive screening outcome (positive/ negative) in 60.0%, with an overall concordance of 85.2% compared with standard PA screening. Among 19 patients classified as negative by the Mulatero flowchart, two were positive on standard screening, indicating potential missed PA cases. The ES flowchart provided a definitive classification in 12 patients (15.6%), with 91.7% concordance with standard screening. All patients classified as negative by the ES flowchart were also negative according to standard screening.

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Kinetics of β -Cell function in cystic fibrosis using HOMA2 indices

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Abstract

Objective

Screening for cystic fibrosis-related diabetes (CFRD) using the oral glucose tolerance test (OGTT) classifies patients according to glucose tolerance categories. Longitudinal analysis of HOMA2 indices could be applied to estimate the decline in β -cell function and identify patients at increased risk of developing CFRD without the need for a burdensome dynamic test (1).

Materials, patients and Methods

Screening for cystic fibrosis-related diabetes (CFRD) using the oral glucose tolerance test (OGTT) classifies patients according to glucose tolerance categories. Longitudinal analysis of HOMA2 indices could be applied to estimate the decline in β -cell function and identify patients at increased risk of developing CFRD without the need for a burdensome dynamic test (1).

Results

HOMA2-%B (β -cell function) was significantly lower in progressors than in non-progressors ($b = -26.8$ pp, $p = 0.049$), and its rate of decline with age did not differ significantly between groups. In contrast, progressors showed significantly higher levels for HOMA2-%S and the HOMA2 hyperbolic product ($\text{HOMA2-\%B} \times \text{HOMA2-\%S}$) ($bS = 52.9$ pp, $pS = 0.005$; $bB \times S = 21.15$ pp, $pB \times S = 0.091$) and their decline with age were significantly faster ($pS = 0.041$, $pB \times S = 0.026$): 1.3% annual decline in progressors compared with 0.26% in non-progressors.

Conclusion

Longitudinal assessment of the HOMA2 hyperbolic product helps identifying patients at increased risk of progression to CFRD, through its accelerated rate of decline. It represents a simple, non-invasive tool that may complement OGTT for risk stratification in patients with cystic fibrosis.

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Low measured free testosterone is associated with worse sexual function in community-dwelling men

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Objective

Lower free testosterone (T) appears more strongly associated with male sexual dysfunction than total T, but most evidence is based on calculated free T (cFT) rather than measured free T (mFT). This study examined associations between mFT and sexual function in community-dwelling men. Design: Cross-sectional analysis of 526 European Male Ageing Study (EMAS) participants.

Methods

Sexual function in EMAS was assessed through a validated sexual function questionnaire. mFT was measured by liquid chromatography tandem mass spectrometry (LC-MS/MS) following equilibrium dialysis. Vermeulen-derived cFT was calculated from LC-MS/MS total T and sex-hormone binding globulin. Associations of sexual outcomes with total T, cFT and mFT were analysed using proportional ordinal logistic regression and restricted cubic splines adjusted for age, body mass index (BMI) and centre.

Results

The mean age in this EMAS study group was 70.5 ± 8.5 years, with a mean body mass index of 27.3 ± 3.3 kg/m², mean total T of 16.7 ± 6.3 nmol/L, mean cFT of 269.2 ± 86.6 pmol/L and mean mFT of 197.7 ± 82 pmol/L. Lower mFT was significantly associated with erectile dysfunction (odds ratio (OR) per 10 pmol/L decrease 1.04 [1.01 - 1.06]), fewer sexual intercourse (OR 1.03 [1.00 - 1.06]), lower orgasm frequency (OR 1.03 [1.01 - 1.06]) and reduced sexual desire (OR 1.03 [1.01 - 1.05]). Total T was not associated with any outcome and cFT only with erectile dysfunction (OR per 10 pmol/L decrease 1.03 [1.01 - 1.05]) and reduced sexual desire (OR 1.03 [1.00 - 1.05]). Non-linear associations were observed for mFT with erectile function and orgasm frequency, with markedly steeper increase in predicted probability of worse functioning below 163 and 138 pmol/L, respectively (Figure 1).

Conclusion

In community-dwelling men, lower mFT was associated with worse erectile function, fewer sexual intercourse attempts, reduced orgasm frequency, and lower sexual desire, with apparent non-linear thresholds for erectile dysfunction and orgasm frequency at 163 and 138 pmol/L, respectively.

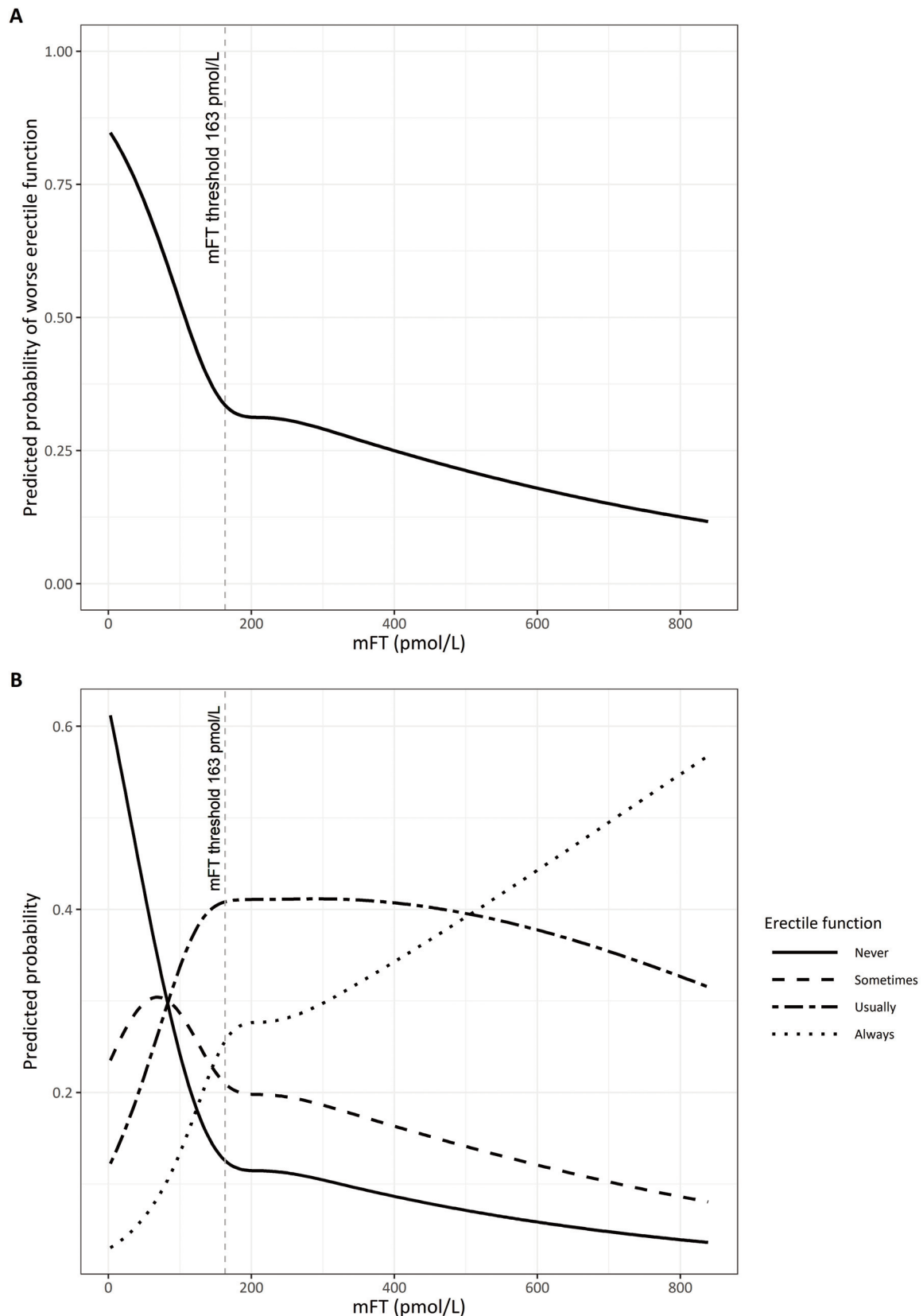


Figure 1. Predicted probabilities of erectile function across the distribution of mFT. The vertical dashed line indicates the estimated mFT level (163 pmol/L), below which a further decrease in mFT is associated with a steeper increase in the probability of reporting worse erectile function.

(A) Predicted probability of worse erectile function, defined as outcome categories “Never” and “Sometimes”. (B) Predicted probabilities for each erectile function level separately.

Current trend in neonatal blood spot TSH suggests normal iodine status of the Flemish population

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Abstract

Introduction

Neonatal thyroid-stimulating hormone (TSH), measured in dried blood spots (DBS) during routine screening for congenital hypothyroidism, is widely used as a pragmatic indicator of population iodine status. However, its interpretation requires consideration of perinatal, seasonal, and methodological influences. We assessed iodine status in Flanders using neonatal DBS TSH concentrations and examined temporal trends and determinants of variation.

Methods

In this retrospective population-based cohort study, we analysed anonymised DBS TSH data from 174,027 term neonates (37-41 weeks of gestation) born in Flanders between 2020 and 2023. Samples were obtained on day 3 or 4 of life and included if TSH was <15 mIU/L (the cutoff for screen-positive samples). TSH was measured at two screening centres using the same time-resolved fluorometric immunoassay (GSP, PerkinElmer). We calculated the proportions of neonates with TSH >5 mIU/L and >2 mIU/L and evaluated associations with sex, gestational age, birthweight, province, season, sampling day, and year of birth.

Results

Among 174,027 neonates (50.8% male; 69.3% sampled on day 3), mean TSH was 1.90 ± 1.25 mIU/L and differed between screening centres (1.69 vs 2.08 mIU/L; $P<0.001$). Overall, 2.6% of neonates had TSH >5 mIU/L and 33.8% had TSH >2 mIU/L. TSH concentrations were higher in day 3 compared with day 4 samples ($P<0.001$). Mean TSH increased modestly with gestational age ($P<0.001$); each additional week was associated with a 5% higher odds of TSH >2 mIU/L (OR 1.05; $P<0.001$), but not with TSH >5 mIU/L. Neonates with birthweight <2500 g had a higher prevalence of TSH >5 mIU/L ($P<0.001$). Marked seasonal variation was observed, with higher proportions above both thresholds in winter and spring ($P<0.001$). Provincial differences were significant ($P<0.001$). Across the study period, the annual proportion of TSH >5 mIU/L remained below 3%. A significant temporal decline in TSH was observed for both thresholds ($P<0.001$), independent of season and sampling day, although absolute changes were small.

Conclusion

Neonatal TSH distributions in Flanders since 2020 are consistent with iodine sufficiency when applying the >5 mIU/L criterion (2.6%, ref. $<3\%$). TSH concentrations are influenced by season, sampling day, birthweight, and geographic region, underscoring the importance of methodological standardisation when using neonatal TSH to monitor population iodine status.

Associations between 25-OH-vitamin D and sexual function outcomes in the European Male Ageing Study (EMAS)

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Abstract

Background

Evidence associating vitamin D with male sexual function in men remains inconsistent, and few population-based studies have assessed multiple sexual function outcomes using standardized vitamin D measurements. The European Male Ageing Study (EMAS) provides a unique opportunity to address these limitations through its large, multi-national, population-based design; validated, self-administered sexual function questionnaire; and 25-OH-vitamin D (25(OH)D) values adjusted to align DiaSorin measurements with LC-MS/MS reference standards (NIST) (1).

Objective

We aimed to examine associations between serum (total and calculated free) 25(OH)D and five sexual function symptoms in EMAS: sexual thoughts, sexual desire, morning erections, erectile function, and sexual satisfaction.

Methods

We performed a cross-sectional analysis of EMAS data from 2,145 participants with available NIST-corrected 25(OH)D and sexual function measures, assessed using the self-administered EMAS Sexual Function Questionnaire. Ordinal logistic regression models estimated odds ratios (ORs, 95% CI) per 10 ng/mL increase in total and per 1 pg/mL increase in calculated free 25(OH)D, with linearity of the continuous vitamin D terms evaluated using spline models. Lower categories of sexual function measures represent worse sexual function. Multivariable models were adjusted for age, BMI, smoking status, and study centre. Additional analysis included a vitamin D cut-off of <20 versus $\geq$ 20 ng/mL.

Results

Participants had a median age of 57.3 years (IQR 49.1–66.6); vitamin D and calcium supplement use was rare (0.56%). Total 25(OH)D was significantly associated with erectile function and morning erections in both unadjusted and adjusted models. Spline models did not improve model fit, and vitamin D was therefore retained as a linear continuous predictor. Adjusted ORs were 1.15 (95% CI 1.04–1.26) for erectile function and 1.20 (95% CI 1.10–1.31) for morning erections, and these associations remained consistent in additional analysis using a vitamin D cut-off of 20 ng/mL. Associations for sexual thoughts, sexual desire, and satisfaction were attenuated after adjustment. Free 25(OH)D showed similar patterns, with significant associations for erectile function (OR 1.06, 95% CI 1.02–1.10), morning erections (OR 1.08, 95% CI 1.04–1.12), and sexual desire (OR 1.04, 95% CI 1.00–1.08) after adjustments.

Conclusion

In this large, multi-centre European cohort with NIST-standardized vitamin D measurements and a validated multidimensional sexual function questionnaire, higher total and free 25(OH)D were consistently associated with better erectile function outcomes, particularly morning erections. Free 25(OH)D did not provide meaningful additional predictive value beyond total 25(OH)D. Overall, these findings support 25(OH)D as a biomarker of male sexual function, especially erectile function outcomes, in middle-aged and older men.

References

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doi: 10.1111/j.1365-2605.2008.00879.x

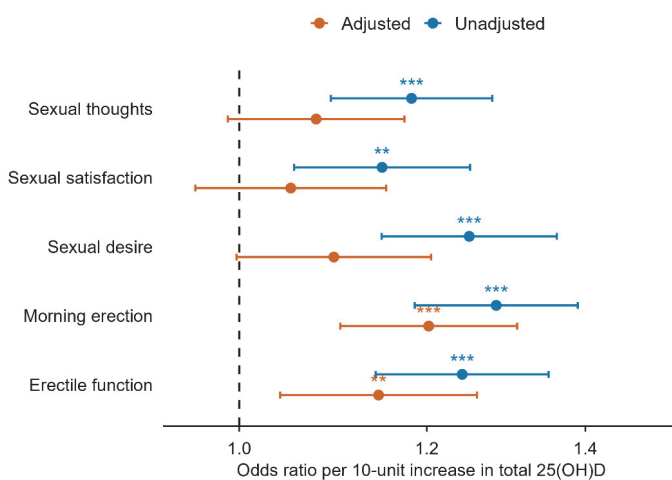


Figure 1. Association between sexual function outcomes and total 25(OH)D (continuous). Forest plot showing unadjusted (blue) and adjusted (red) odds ratios per 10-ng/mL increase in total 25(OH)D. Adjusted models include age, centre, BMI, and smoking. * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$

Sensitivity analyses for associations between vitamin D and sexual function outcomes

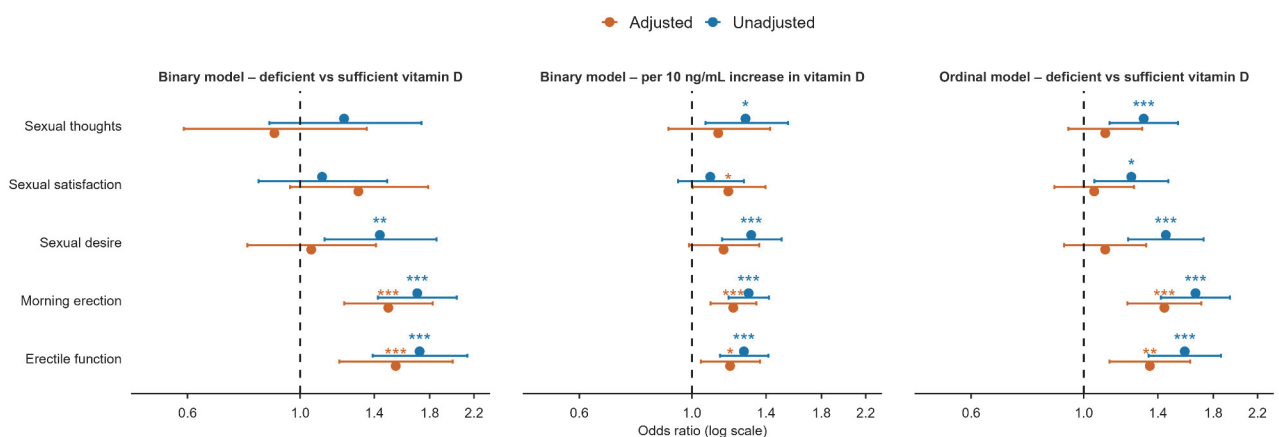


Figure 2. Robustness of the association between sexual function outcomes and total 25(OH)D. Forest plot showing unadjusted (blue) and adjusted (red) odds ratios across sensitivity models. Sexual function outcomes were modelled as ordered or binary, and total 25(OH)D as continuous (per 10-ng/mL) or dichotomous (deficient < 20 vs sufficient ≥ 20 ng/mL). Adjusted models include age, centre, BMI, and smoking. * $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$

Cytokine dynamics following initiation of gender-affirming hormone therapy in transgender subjects

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Abstract

Background

Sex is an important determinant for various immune system-related pathologies and sex steroids might possess immunomodulatory properties.

Objective

To study the effects of sex steroid exposure on the serum levels of immune-related biomarkers (irBMs), using a model of transgender individuals receiving genderaffirming hormone therapy (GAHT).

Material and methods

Serum samples were collected from hormone-naïve trans women (TW) (n=30) and trans men (TM) (n=30) who initiated GAHT at baseline and after ± 6 months of treatment. Cisgender men (n=10) and cisgender women (n=10) were included as controls. High-sensitivity C-reactive protein (hs-CRP) was measured using immunoassay. Serum levels of several irBMs, including cytokines and chemokines were determined using a commercial multiplex assay (Olink®). Serum estradiol and testosterone were determined using liquid-chromatography tandem mass spectrometry (LC-MS/MS).

Results

After ± 6 months of GAHT in TW, serum levels of ten cytokines (CCL2, CCL7, CCL11, CCL13, CCL19, CXCL9, CXCL10, CXCL11, IL15 and TNFSF10) significantly decreased, whereas IL7 increased. In TM, eight factors significantly increased (CCL2, CCL7, CCL11, CCL13, CCL19, IL17C, MMP1 and TNFSF10). Further, a hierarchical clustering of the fold-change data of significant irBMs shows that changes in different irBMs might be linked together. In TM, a prominent cluster comprised CCL2, CCL11 and CCL13. In TW, a similar strong cluster could be seen in CXCL9, CXCL10 and CXCL11, and one in TNFSF10 and CCL19. Other immune-related biomarkers were not significantly affected, and levels of hs-CRP did not show a clinically relevant change over time.

Conclusion

Six months of estrogen with antiandrogen treatment resulted in decreased serum levels of several cytokines and chemokines in TW, whereas cytokine and chemokine levels often increased in TM upon treatment with testosterone. Furthermore, a clustering of changes was observed among functionally related cyto- and chemokines, indicating shared regulatory mechanisms.

These distinct and generally opposite changes suggest a sex steroid-dependent impact, which could contribute to sex-related disparities in (auto)immune diseases. However, additional research should explore potential clinical consequences, as well as the mechanisms involved.

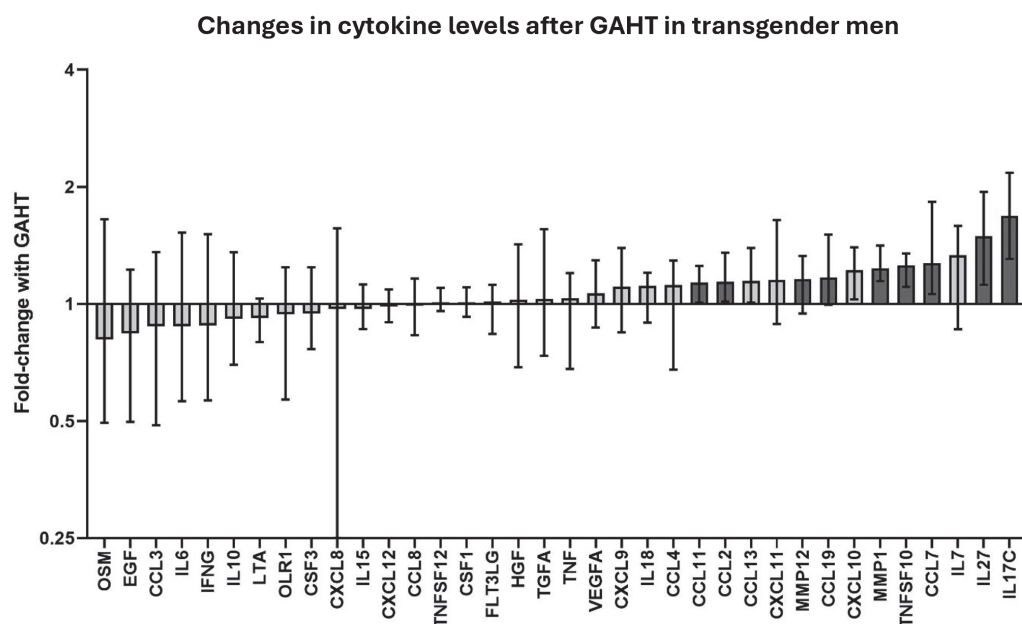


Figure 1. Comparative analysis of biomarkers levels at baseline and after approximately six months of treatment with testosterone undecanoate in transgender men. Fold changes versus baseline are shown. Biomarkers that were significantly different after correction for multiple testing (Holm-Bonferroni) are dark shaded. Biomarkers were sorted along the X-axis based on their effect, ranking from biggest decrease to biggest increase.

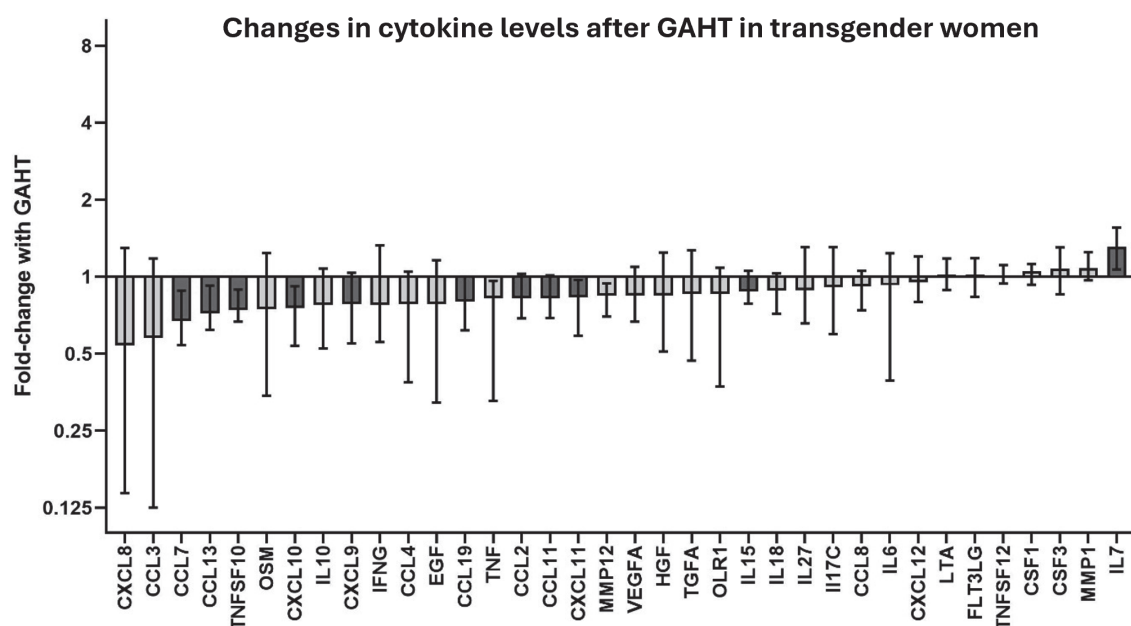


Figure 2. Comparative analysis of biomarkers levels at baseline and after approximately six months of treatment with estrogens with 12.5 – 25 mg cyproterone acetate in transgender women. Fold changes versus baseline are shown. Biomarkers that were significantly different after correction for multiple testing (Holm-Bonferroni) are dark shaded. Biomarkers were sorted along the X-axis based on their effect, ranking from biggest decrease to biggest increase.

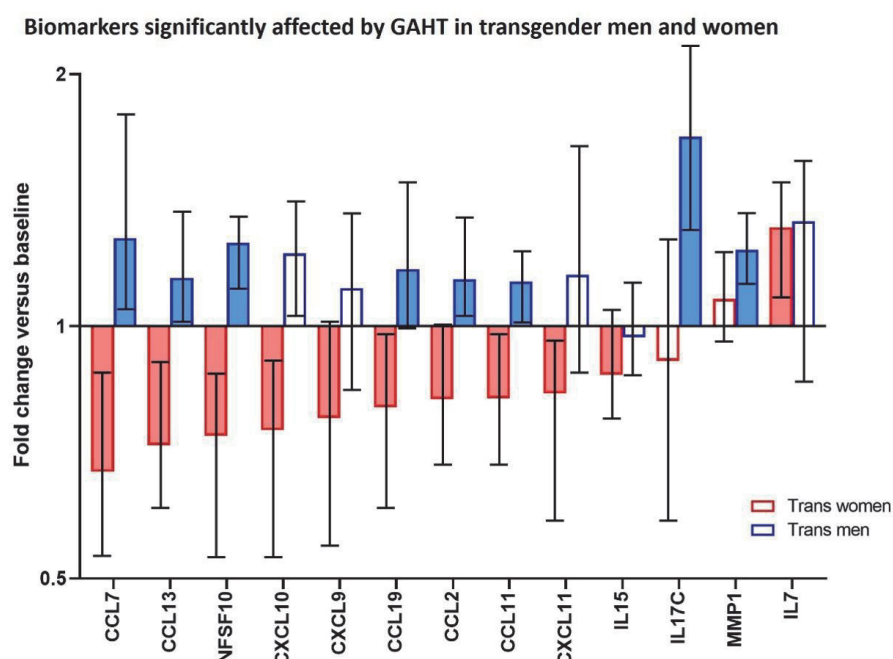


Figure 3. An overview of irBMs that were significantly affected by GAHT in TM TW. Dark grey bars indicate effects in TM, whereas grey bars indicate TW. Bars with an asterisk indicate that the effect was statistically significant after correction for multiple testing. Cytokines were sorted according to the effect in TW, ranking from greatest decrease to greatest increase.

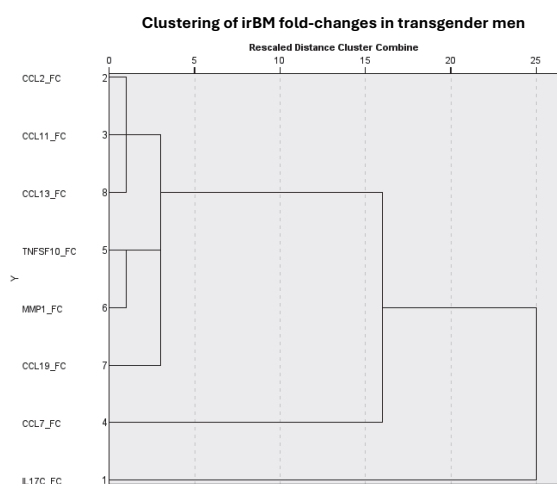


Figure 4. This dendrogram shows possible clusters of fold changes of irBMs in transgender men. Vertical axis: Fold changes in chemo/cytokines (only irBMs with significant changes are shown), horizontal axis: rescaled distance. FC: fold-change, irBM: immune-related biomarkers.

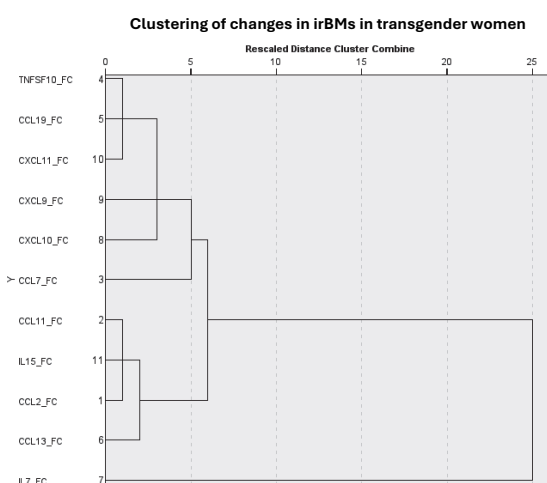


Figure 5. This dendrogram shows possible clusters in changes in irBMs in transgender women. Vertical axis: Fold changes in chemo/cytokines (only irBMs with significant changes are shown), horizontal axis: rescaled distance. FC: fold-change, irBM: immune-related biomarkers.

Giant pheochromocytomas: clinical presentation and perioperative outcomes

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Abstract

Background

Giant pheochromocytomas, defined as tumors measuring ≥ 7 cm, are uncommon, and their clinical presentation, perioperative management and postoperative outcomes remain poorly characterized.

Objective

To compare the clinical presentation and perioperative outcomes of patients with giant versus non-giant pheochromocytomas.

Methods

We conducted a retrospective single-center cohort study including all consecutive patients who underwent surgical resection of a pheochromocytoma at Cliniques Universitaires Saint-Luc (Brussels, Belgium) between January 1, 1998, and August 10, 2025.

Results

Among 102 patients, 22 (21.6%) had giant pheochromocytomas with a mean tumor diameter of 10.1 cm. Patients with giant tumors had significantly higher levels of 24-hour urine metanephrines (median $14.8 \times \text{ULN}$ vs $2.4 \times \text{ULN}$, $p=0.018$) and normetanephrines ($15.8 \times \text{ULN}$ vs $2.6 \times \text{ULN}$, $p=0.001$) compared to tumors < 7 cm. Giant pheochromocytomas were associated with a higher prevalence of metastatic disease (25% vs 3%, $p=0.006$), increased perioperative complications (50% vs 15%, $p=0.001$), and longer postoperative hospital stays (10 ± 6 vs 7 ± 5 days, $p=0.010$). Although hypertension (86% vs 66%), diabetes mellitus (64% vs 41%), recurrence (17% vs 10%), and contralateral pheochromocytoma (24% vs 13%) were more frequent in patients with giant tumors, these differences were not statistically significant. Age at diagnosis, sex distribution, and prevalence of germline mutations were similar between groups.

Conclusion

Giant pheochromocytomas are associated with greater catecholamine excess, a higher prevalence of metastatic disease, and increased perioperative complications compared with non-giant tumors. Their longer postoperative hospital stay further reflects the complexity of perioperative management.

Long-term real-world impact of automated insulin delivery on safety, glycemic and parent-reported outcomes in children aged 2 to 6 years with type 1 diabetes

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Abstract

Purpose of the study

This study evaluated the 24-month real-world safety and impact of Medtronic MiniMed™ 780G (780G) on glycemic management and parent-reported outcomes (PROs) in young children with type 1 diabetes (T1D).

Methods

Children aged 2-6 years whose parents agreed to enable 780G were included. Data were collected from before start of 780G and every 3 months to 24 months after. PROs were evaluated with HAPPI-D and Hypoglycemia Fear Survey-II – Parent version [HFS] questionnaires. Data are reported as mean $\pm$ SD or least-squares mean (95% CI), with p-values vs start.

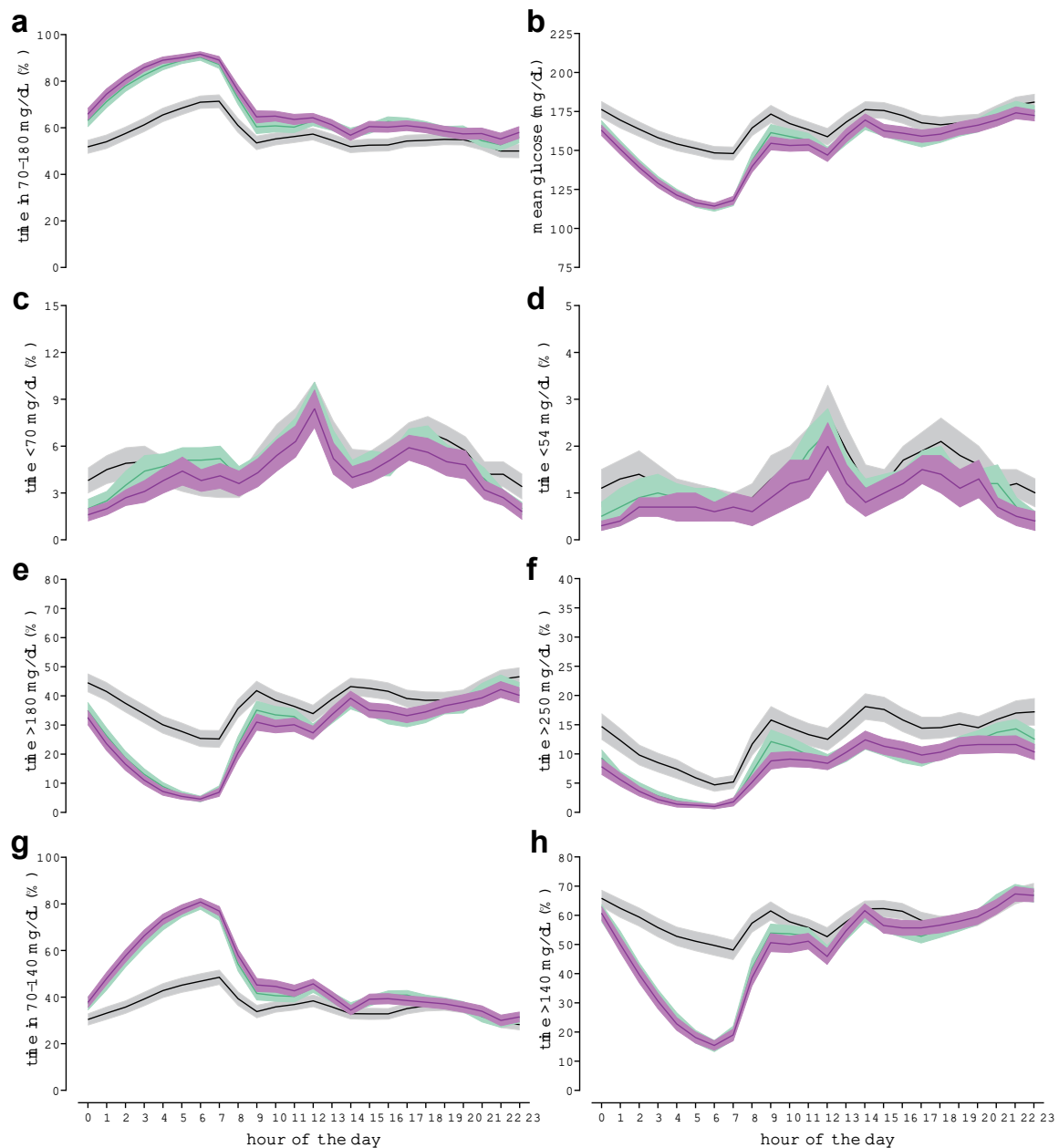
Results

Children (n=149) were 4.2 ± 1.4 years old, 56.4% were girls and 137 completed 24 months of 780G. Time in range 70-180 mg/dL increased from start (56.7% [54.3-59.1]) to 12 months (66.4% [64.4-68.3]) and 24 months (68.0% [66.1-70.0]), with a similar trend for time in tight range 70-140 mg/dL (35.9% [33.5-38.4] to 46.3% [44.1-48.4] and 47.3% [45.3-49.6]) (all $p < 0.001$). HbA1c decreased from 7.6% (7.4-7.8) at start to 7.3% (7.1-7.5) at 12 months and 7.2% (7.0-7.4) at 24 months ($p < 0.001$). Time in hyper- and hypoglycemia also improved from start to 12 months and remained stable up to 24 months, while the coefficient of variation did not change during the study (40.0% [39.2-40.9] at start to 41.2% [40.3-42.0] at 12 months and 40.3% [39.4-41.2] at 24 months, $p = 0.820$). Notably, mean time spent within and outside specific target ranges showed greater improvements during nighttime than daytime and a persistent increase in mean time spent in hypoglycemia was seen at 12:00 PM and an increase in mean time spent in hyperglycemia in the evening (Figure 1). As to PROs, children's quality of life (HAPPI-D) and parents

fear of hypoglycemia (HFS-worry) improved from start to 12 months and remained stable until 24 months. Similar trends were observed for school absenteeism (728 [458-1156] at start to 396 [292-536] at 12 months and 304 [202-420] days/100 person-years at 24 months, $p=0.002$) and parental work absenteeism (722 [324-1610] at start to 464 [188-1146] at 12 months and 201 [92-441] days/100 person-years at 24 months, $p<0.001$). Two hospitalizations due to diabetic ketoacidosis occurred both during the study and in the preceding year.

Conclusion

In young children with T1D, 24 months use of 780G was safe and improved glycemic management, PROs and school absenteeism, supporting its sustained real-world benefits.



The impact of malnutrition on wound healing and clinical outcomes in patients with diabetic foot ulcers

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Abstract

Study design and objective

Diabetic foot ulcers (DFUs) are a major complication of diabetes mellitus and are associated with impaired wound healing, amputation, and increased mortality. Malnutrition has emerged as a potentially modifiable risk factor that may adversely affect wound healing, yet its prognostic significance in patients with DFUs remains insufficiently investigated. This study aimed to evaluate the impact of malnutrition, diagnosed according to the Global Leadership Initiative on Malnutrition (GLIM) criteria, on wound healing, amputation, and mortality in patients hospitalized with diabetic foot ulcers.

Methods

A retrospective single-centre cohort study was conducted including 222 patients admitted to the University Hospital Antwerp (Belgium) with a diabetic foot ulcer between June 2016 and June 2024. Nutritional status was assessed within 48 hours of admission using the GLIM criteria, incorporating body composition analysis by bioelectrical impedance analysis (BIA). The primary outcome was time to complete wound healing without amputation. A secondary healing outcome included healing after minor amputation, reflecting preservation of a functional limb. Additional outcomes were time to amputation and all-cause mortality. Time-to-event analyses accounting for competing risks were performed using Fine–Gray regression models.

Results

One-third of the study population met the GLIM criteria for malnutrition, with approximately half of these patients classified as severely malnourished. Conventional screening parameters, including body mass index and unintentional weight loss, failed to identify a substantial proportion of malnourished patients, highlighting the added value of objective assessment of muscle mass. Although malnutrition was associated with greater ulcer severity at presentation, it was not independently associated with time to wound healing, amputation, or mortality. The cumulative incidence of wound healing without amputation was 35.4% at 6 months and 41.6% at 1 year, increasing to 70.0% and 76.2%, respectively, when healing after minor amputation was included. Nearly two-thirds of patients underwent at least one amputation during follow-up, predominantly within the first months after inclusion. One-year and five-year overall survival rates were 91.6% and 64.1%, respectively.

Conclusions

Malnutrition, as defined by the GLIM criteria, was highly prevalent among hospitalized patients with diabetic foot ulcers and predisposed to more severe ulcers, but was not independently associated with wound healing, amputation, or mortality in our cohort. These findings suggest that the clinical course of diabetic foot ulcers is predominantly determined by ulcer severity and other comorbidities. The negative impact of malnutrition may also have been partly attenuated by systematic nutritional interventions initiated after the diagnosis of malnutrition. Future prospective studies should evaluate the impact of targeted nutritional interventions while incorporating a more comprehensive assessment of malnutrition, including functional measures such as muscle strength, to better define its prognostic significance.

Acute and long-term impact on the brain of tight versus liberal blood glucose control in corticosteroid-treated critically ill patients

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Background

Early parenteral nutrition (PN) aggravates hyperglycemia and harms intensive care unit (ICU) patients. Corticosteroid use in ICU also aggravates hyperglycemia and associates with delirium, and both hyperglycemia and delirium are linked with long-term mental health problems. We hypothesized that corticosteroid-treated patients represent a vulnerable subgroup that particularly benefit from TGC to reduce hyperglycemia-induced acute and long-term harm to the brain.

Methods

In this secondary analysis of the multicenter TGC-Fast trial (Clinicaltrials.gov-NCT03665207) (1), in which patients not receiving early PN were randomized to TGC (blood glucose 80-110 mg/dL) or liberal blood glucose control (LGC, accepting hyperglycemia up to 215 mg/dL), we assessed whether baseline corticosteroids -identified by corticosteroids initiated within the first two ICU days-, statistically interacted with randomization for its impact on acute and two-year outcomes. In case of a significant interaction, the effect of the randomized intervention was further studied for the corticosteroid-treated and non-corticosteroid-treated subgroups separately, unadjusted and adjusted for baseline risk factors.

Results

Of 9230 patients, 2293 (24.8%) received baseline corticosteroids. Among corticosteroid-treated patients, mean blood glucose concentrations in the first ICU week decreased from 151 (133-169) mg/dL with LGC (being 6.3% higher than for non-corticosteroid-treated patients, $P < 0.0001$) to 116 (108-128) mg/dL with TGC ($P < 0.0001$). Baseline corticosteroids interacted with randomization for in-ICU delirium, two-year mental health outcomes, and mortality. Among corticosteroid-treated patients, TGC reduced delirium from 33.1% to 27.5% in the first ICU week ($P = 0.0051$). At two-year follow-up, TGC improved SF-36 mental component scores ($P = 0.015$), and sub-scores for vitality ($P = 0.041$) and mental health ($P = 0.032$), and reduced mortality from 32.8% to 28.7% ($P = 0.034$). In non-corticosteroid-treated patients, these effects were not present. Results were similar after adjustment for baseline risk factors.

Conclusion

Corticosteroid use increased the severity of hyperglycemia in ICU patients and for corticosteroid-treated patients, TGC reduced the incidence of in-ICU delirium, and improved two-year mental health outcomes and survival.

References

1. Gunst J, Debaveye Y, Güiza F, et al. Tight Blood-Glucose control without Early Parenteral Nutrition in the ICU. *N Engl J Med*. 2023; 389(13):1180–1190. doi:10.1056/NEJMoa2304855

Impact of tight versus liberal blood glucose control in the absence of early parenteral nutrition on neurological injury and two-year outcome in neurointensive care patients

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Background

The multicenter TGC-Fast trial showed, in a context of withholding early parenteral nutrition (PN), that tight blood-glucose control (TGC) may improve acute survival specifically in neurointensive care patients as compared with liberal blood-glucose control (LGC) (1). We hypothesized that TGC, while avoiding hypoglycemia, reduces neurological injury and improves long-term outcome in these patients.

Methods

In this pre-planned secondary analysis of TGC-Fast (Clinicaltrials.gov-NCT03665207), we investigated, in neurointensive care patients with an ICU stay of ≥ 7 days and available serum samples (N=233), the impact of TGC versus LGC on biomarkers quantified from days 1 to 7 (S100B and glial fibrillary acidic protein [GFAP] as astrocytic injury markers, neuron-specific enolase [NSE] as neuronal injury marker, and neurofilament light chain [NfL] and brain-derived tau [BD-tau] as axonal injury markers). We included 20 age-, sex- and BMI-matched healthy volunteers as reference. Subsequently, we studied, in all neurointensive care patients in TGC-Fast (N=1053), the impact of randomization on two-year survival and functional outcome (SF-36 survey) by multivariable regression analyses adjusted for baseline risk factors. Missing SF-36-scores were imputed, as inability to complete the SF-36 survey may reflect poor functional outcome.

Results

TGC decreased serum S100B from days 2 to 7 (all $P < 0.05$), and GFAP and NSE from days 3 to 7 (all $P < 0.05$). Likewise, TGC reduced the occurrence of abnormal (above highest healthy volunteer level) peak serum S100B (54.9% vs. 68.5%, $P = 0.034$), GFAP (84.4% vs. 94.6%, $P = 0.012$), and NSE (13.1% vs. 26.1%, $P = 0.012$). At two-year follow-up, TGC improved survival (from 71.2% to 76.4% ($P = 0.048$)), the SF-36 mental component score ($P = 0.020$), and sub-scores for role limitations due to emotional problems ($P = 0.019$) and mental health ($P = 0.031$).

Conclusion

In neurointensive care patients not receiving early PN, TGC, provided with a protocol that avoided hypoglycemia, significantly reduced neurological injury, and improved two-year survival and functional outcome as compared with tolerating hyperglycemia.

References

1. Gunst J, Debaveye Y, Güiza F, et al. Tight Blood-Glucose control without Early Parenteral Nutrition in the ICU. *N Engl J Med*. 2023; 389(13):1180–1190. doi:10.1056/NEJMoa2304855

Redosing of anti-CD3 antibodies in NOD mice with new-onset diabetes does not alter the effect of a single treatment course

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Aims/hypothesis

Uncertainty exists regarding the effectiveness of redosing teplizumab, a humanised anti-CD3 monoclonal antibody, in individuals with stage 2 and 3 type 1 diabetes. This study aimed to investigate the impact of redosing an anti-CD3 antibody on disease reversal and immune responses in NOD mice.

Methods

New-onset diabetic NOD mice were treated with a short course (days 0-4) of low-dose anti-CD3 (2.5 µg/day i.v.), followed by a second treatment course administered either early (days 14-18) or late (days 43-47) following the initial course. Diabetes outcomes, anti-drug antibody titres, inflammatory markers and the profiles of peripheral blood and pancreatic immune cells were assessed.

Results

A single course of anti-CD3 therapy reversed type 1 diabetes in 17 out of 40 treated mice (43%). However, neither early nor late redosing improved therapeutic outcomes in non-responder mice or disrupted re-established tolerance in responder mice. Early redosing, administered at the time of CD3⁺ T cell repopulation, and late redosing, timed when anti-drug antibody titres declined after their peak at 14 days, failed to induce remission in non-responder mice (0/10 and 0/5, respectively). Importantly, redosing did not trigger relapse in mice that had achieved remission following the initial treatment course, with all remaining normoglycaemic (5/5 with early redosing; 23/23 with late redosing). Inflammatory markers increased transiently, regardless of treatment response or regimen. In the pancreas, responder mice had a pronounced shift from an effector (CD62L⁺CD44⁺) to a naive (CD62L⁺CD44⁻) phenotype in both CD4⁺ and CD8⁺ T cells, independent of treatment regimen, indicative of a more regulated immune environment. These mice also exhibited elevated frequencies of CD4⁺ and CD8⁺ T cells with an exhausted (programmed cell death protein 1 [PD1]⁺killer cell lectin-like receptor subfamily G, member 1 [KLRG1]⁺) profile in their pancreas, a trait not observed in non-responder mice. Furthermore, the proportion of natural killer (NK) (NKp46⁺CD3⁻) cells was enriched in the pancreas of non-responder mice.

Conclusions/interpretation

These findings suggest that while a single course of anti-CD3 therapy can be effective in a subset of mice, redosing does not enhance efficacy yet is well tolerated in previously reversed mice.

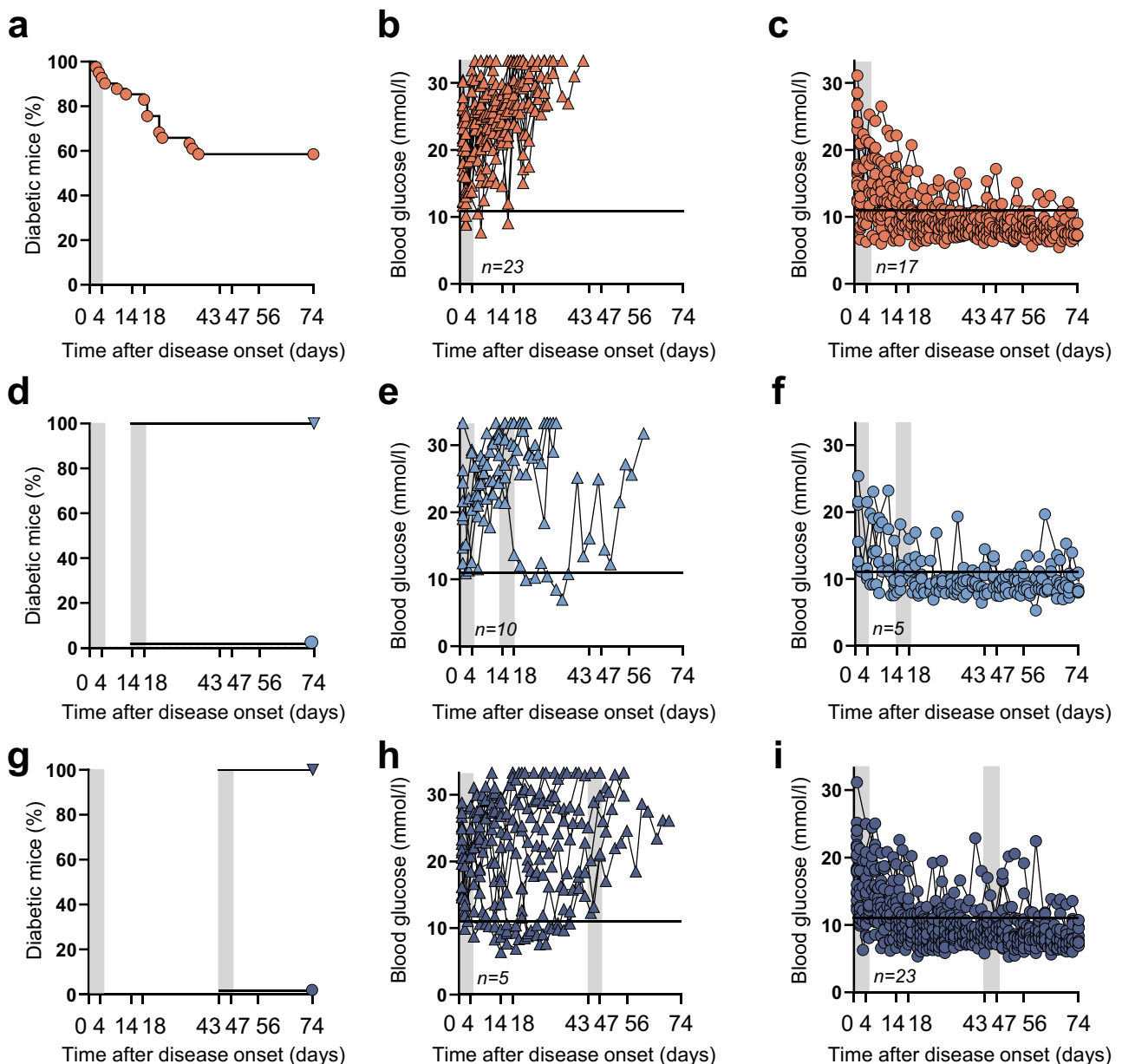


Figure 1: Diabetes reversal after single or repeated anti-CD3 treatment in new-onset diabetic NOD mice. Kaplan-Meier curves show reversal after a single course (a, $n=40$), an early second course (d, $n=15$), or a late second course (g, $n=28$). Blood glucose concentrations are shown for non-responders (b,e,h) and responders (c,f,i). Symbols represent individual mice; numbers indicate mice completing each course. Circles, responders; triangles, non-responders. Grey shading indicates treatment.

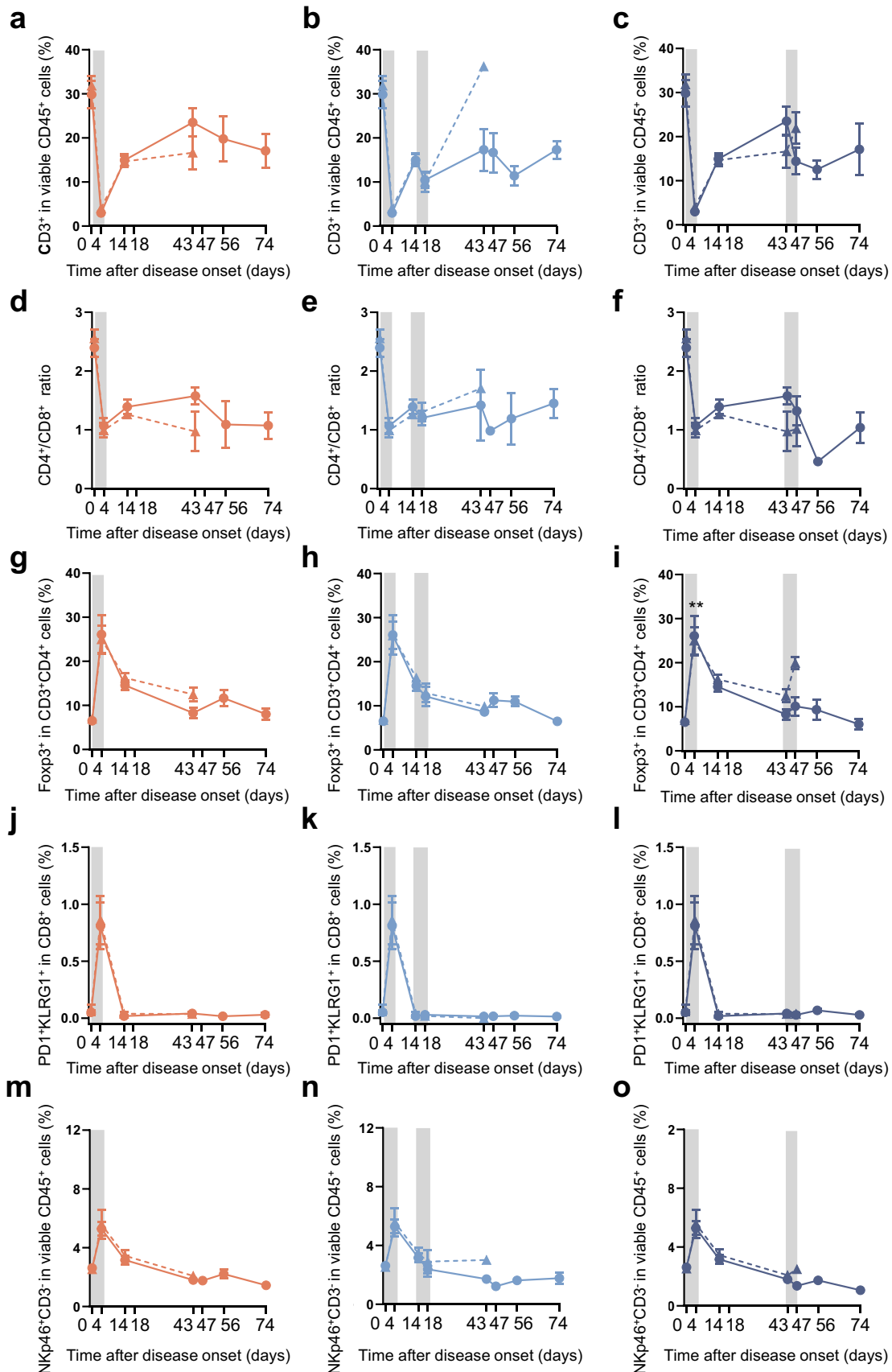


Figure 2: Immunomodulatory effects of anti-CD3 treatment and redosing in peripheral blood. Longitudinal analysis shows frequencies of CD3⁺ T cells (a–c), CD4⁺ to CD8⁺ ratio (d–f), Foxp3⁺CD4⁺ Tregs (g–i), PD1⁺KLRG1⁺CD8⁺ T cells (j–l), and NKp46⁺CD3⁻ NK cells (m–o). Symbols represent group means. Solid lines with closed circles indicate responder mice (n=11); dashed lines with closed triangles indicate non-responder mice (n=19). Grey shading indicates treatment. Mean ± SEM.

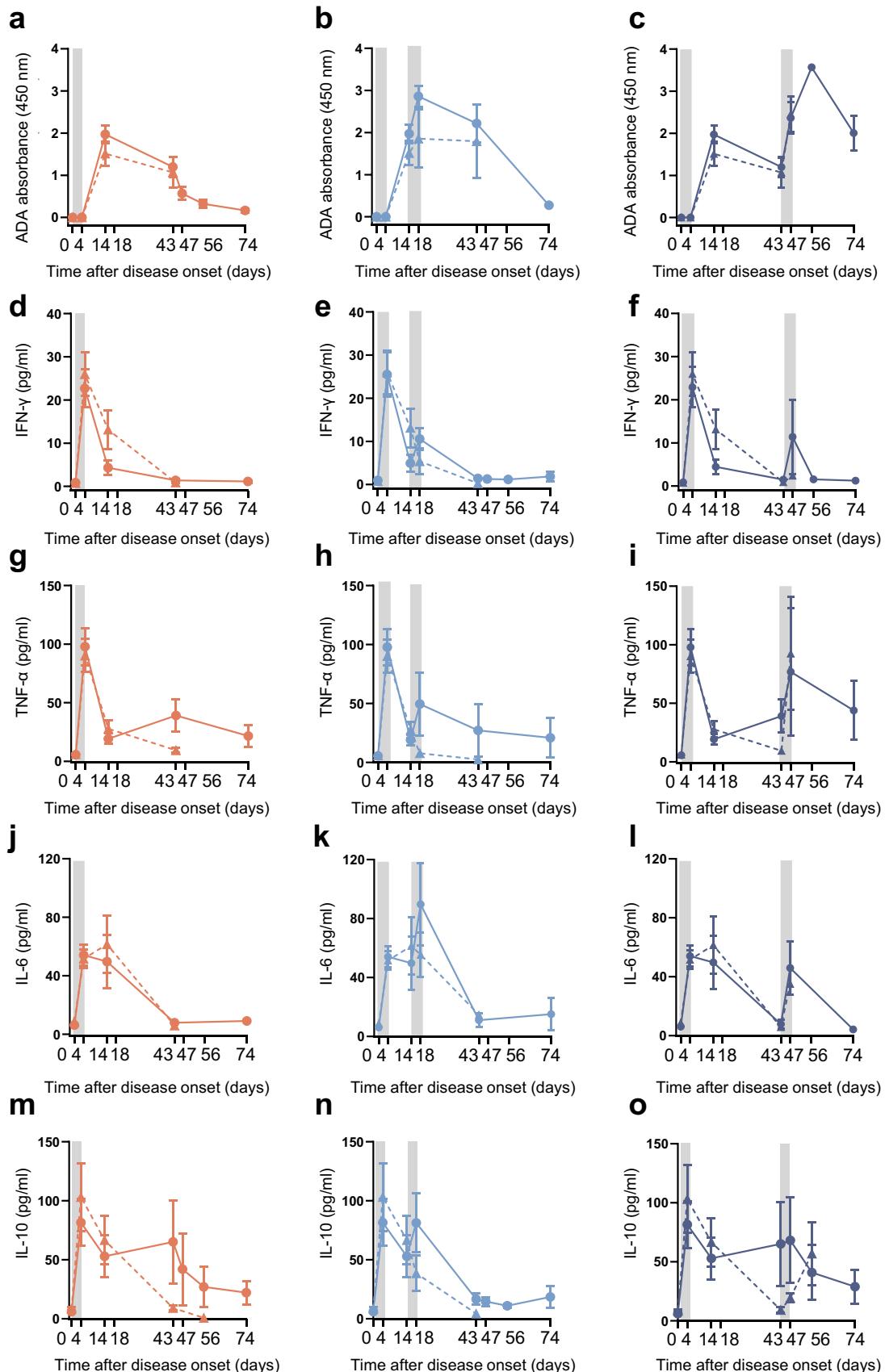


Figure 3: Time course of ADA titres and cytokine responses following anti-CD3 treatment and redosing. ADA titres in 160× diluted plasma (a–c) and plasma concentrations of IFN- γ (d–f), TNF- α (g–i), IL-6 (j–l), and IL-10 (m–o) were measured across treatment regimens. Symbols represent group means. Solid lines with closed circles indicate responder mice (n=11); dashed lines with closed triangles indicate non-responder mice (n=19). Grey shading indicates treatment. Mean $\pm$ SEM.

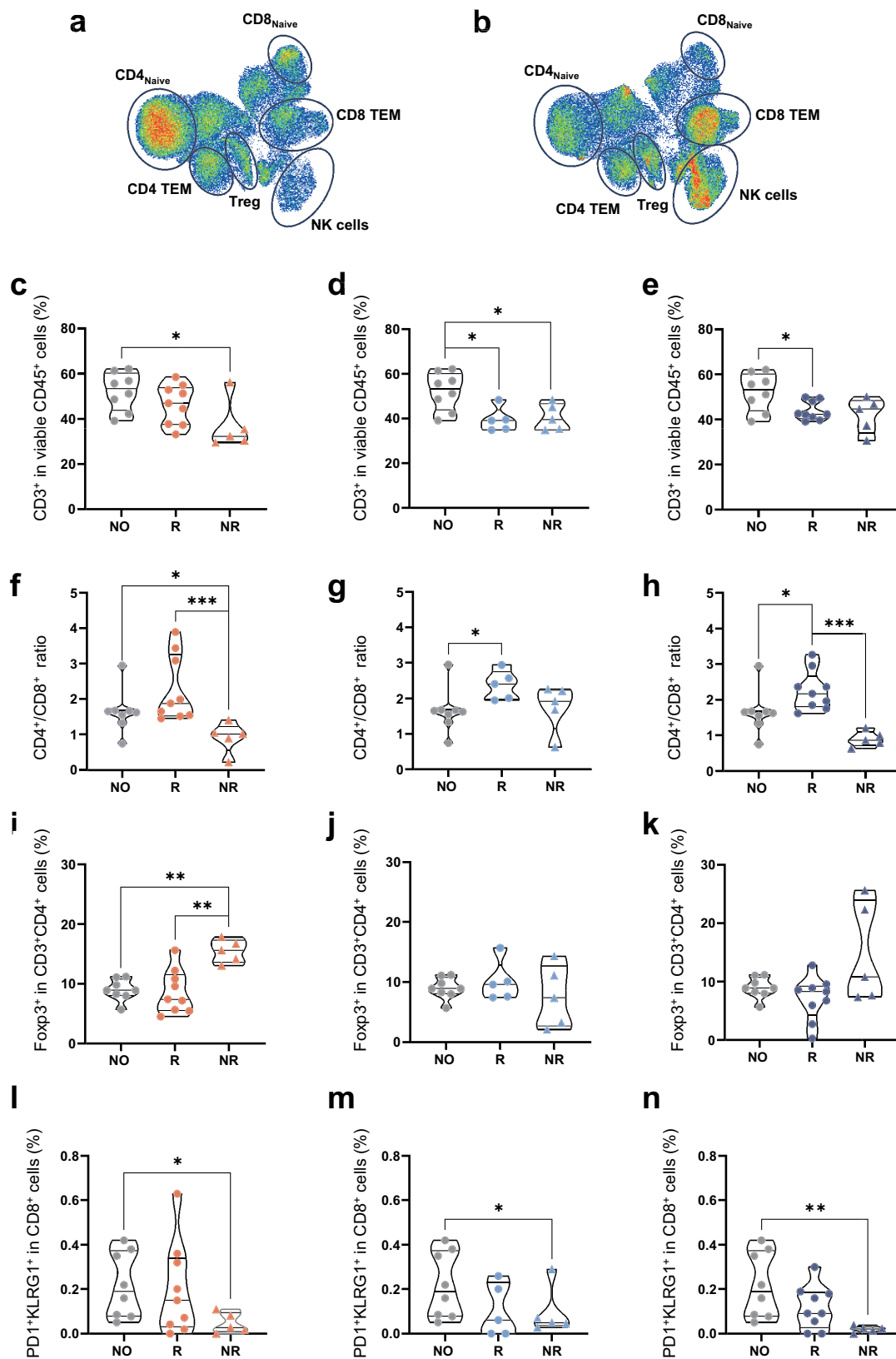


Figure 4: Immunomodulatory effects of anti-CD3 treatment and redosing in the pancreas. UMAP of CD3⁺ T and NK cells split by responder (a) and non-responder (b). Pancreatic frequencies of CD3⁺ T cells (c-e), CD4⁺ to CD8⁺ ratio (f-h), Foxp3⁺CD4⁺ Tregs (i-k), and PD1⁺KLRG1⁺CD8⁺ T cells (l-n). Symbols show individual mice; circles, responders; triangles, non-responders. Violin plots show median and IQR. * $p \leq 0.05$; ** $p \leq 0.01$; *** $p \leq 0.001$ (Mann-Whitney U). NO, new-onset; NR, non-responder; R, responder.

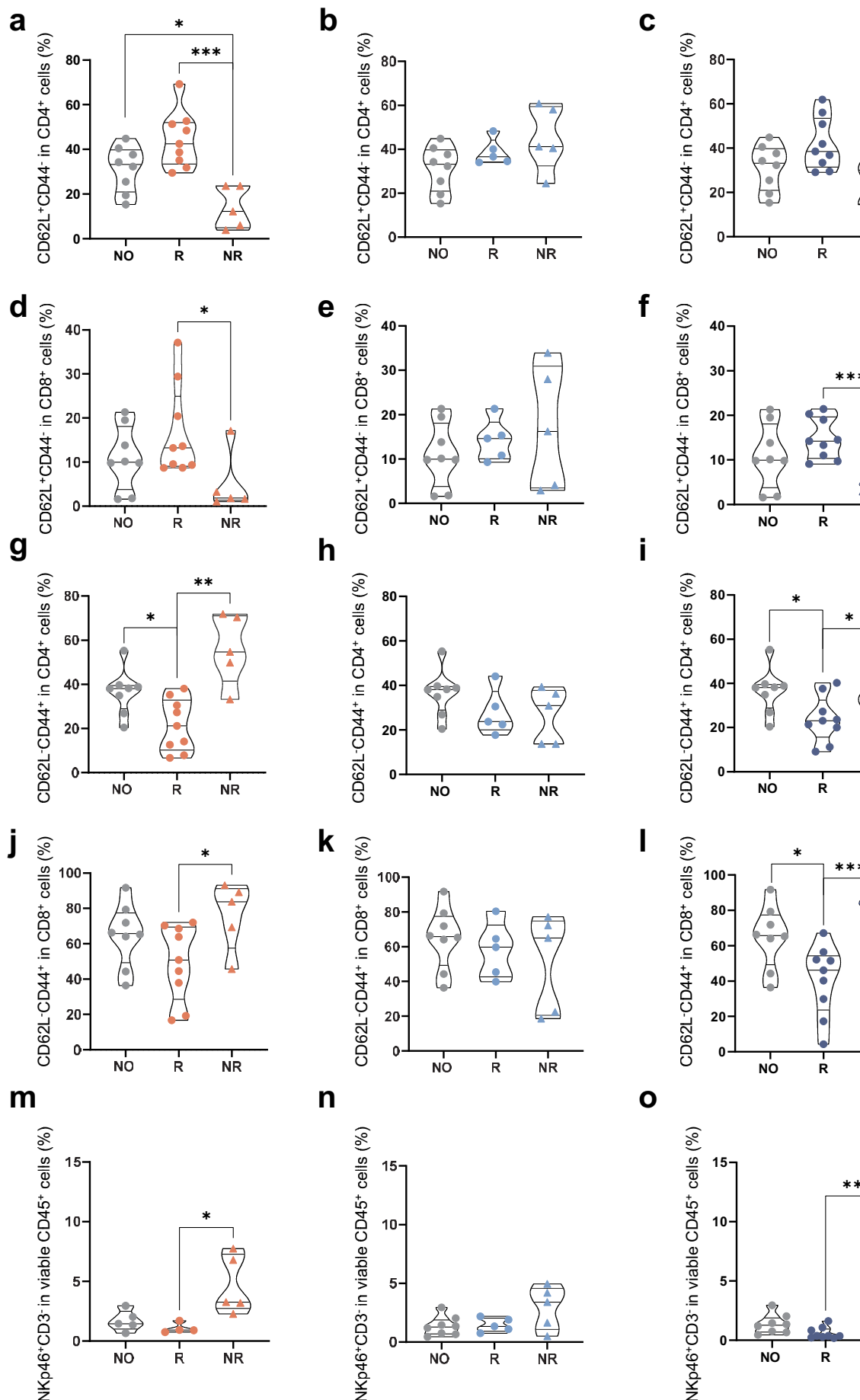


Figure 5: Effect of redosing anti-CD3 on T and NK cell subpopulations in the pancreas. Pancreatic frequencies of CD4⁺ CD62L⁺CD44⁻ (naive) (a–c) and CD62L⁻CD44⁺ (TEM) (g–i), CD8⁺ CD62L⁺CD44⁻ (naive) (d–f) and CD62L⁻CD44⁺ (TEM) (j–l), and Nkp46⁺CD3⁻ NK cells (m–o) at study endpoint. Symbols represent individual mice; circles, responders; triangles, non-responders. Violin plots show median and IQR. * $p \leq 0.05$; ** $p \leq 0.01$; *** $p \leq 0.001$ (Mann–Whitney U). NO, new-onset; NR, non-responder; R, responder.

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CLINICAL CASE REPORTS

Beyond thyroid eye disease: remarkable improvement of refractory pretibial myxoedema with teprotumumab

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Abstract

Background

Pretibial myxoedema (PTM), a rare extrathyroidal manifestation of Graves' disease (GD), affects 0.5–4% of patients and is associated to thyroid eye disease (TED) in 97% of cases. PTM exhibits marked clinical heterogeneity, ranging from classic non-pitting pretibial oedema to nodular, plaque, pseudotumoral and elephantiasic forms. In 43% of cases, PTM presents classic bilateral pretibial involvement, although atypical localization involving the feet, toes, upper extremities, face, or trunk has also been reported. The onset of PTM is often temporally dissociated from Graves' disease. Male sex and older age are associated with more severe PTM. The pathogenesis of PTM shares common immunological mechanisms with GD and TED, with the TSH receptor (TSHR) serving as the principal autoantigen. TSHR is expressed in pretibial connective tissue, where stimulation by TSH receptor antibodies (TSHR-Ab) activates local fibroblasts, leading to inflammation and fibrosis in later stages. PTM activity and severity correlate positively with circulating TSHR-Ab levels. In addition, insulin-like growth factor-1 receptor (IGF-1R) is overexpressed in dermal fibroblasts, supporting the concept of a functional TSHR/IGF-1R signaling complex reminding TED pathogenesis. The characteristic pretibial distribution is thought to result from local mechanical factors, including gravitational and positional forces, repetitive trauma, impaired lymphatic drainage, and the thin skin overlying the anterior tibia. Case: We report the case of an active-smoking woman diagnosed in 2021 with severe GD complicated with TED. She underwent total thyroidectomy in June 2022. She required urgent orbital decompression in December 2022 for TED progression to dysthyroid optic neuropathy, followed by two strabismus surgeries in 2023 and 2024. Shortly after the thyroidectomy, she developed disabling pseudotumoral PTM, despite progressively



Figure 1: Clinical evolution of PTM during Teprotumumab treatment.

declining but persistently elevated TSHR-Ab levels. Teprotumumab treatment was initiated in March 2025, after the failure of tofacitinib therapy, and we observed a rapid and marked improvement of PTM already after the first infusion, with a total of 5-cm reduction in ankle circumference and a decrease in shoe size from 46 to 41, allowing the patient to resume wearing standard footwear. The toe lesions showed a more limited response and were successfully managed with adjunctive intralesional high potency corticosteroid therapy. Treatment was discontinued after the seventh infusion for fatigue at the patient's request. Mild unilateral sensorineural hearing impairment developed after the second infusion, remained stable throughout treatment and completely recovered after the treatment discontinuation.

Conclusion

This case illustrates the severe functional disability that PTM can cause despite definitive treatment of hyperthyroidism. The marked improvement following IGF-1R inhibition supports the shared pathophysiology of PTM and TED and suggests that teprotumumab may represent a promising therapeutic option for refractory PTM. Standardized clinical outcome measures and prospective studies are needed to better define treatment efficacy and guide management of this rare disorder.

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Bloom syndrome presenting as early-onset bilateral breast cancer and multisystem metabolic disease: a case report

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Abstract

Bloom syndrome is a rare autosomal recessive disorder caused by pathogenic variants in the BLM gene and is characterized by early-onset malignancy, growth deficiency, metabolic abnormalities, and cutaneous findings. We report the case of a 33-year-old woman with bilateral early-onset breast cancer, lipodystrophy, severe hypertriglyceridemia complicated by pancreatitis, and type 2 diabetes mellitus. Initial targeted genetic testing did not identify a causative variant. Comprehensive multigene testing subsequently revealed a homozygous likely pathogenic splice-site variant in BLM (c.98+1G>T), establishing the diagnosis of Bloom syndrome. This case expands the clinical and genetic spectrum of Bloom syndrome and illustrates that targeted cancer gene panels can fail to detect syndromic cancer predisposition disorders, leading to diagnostic delay. Expanded genetic testing should be considered early in patients with multiple primary malignancies accompanied by suggestive syndromic features, as timely diagnosis enables syndrome-adapted management, tumor surveillance, and family counseling.

Gene	Transcript	Chr	Position	Exon	Coding	Status	Evaluation
BLM	NM_000057	15	90747491	2	c.98+1G>T	HOM	4 - Probably pathogenic

Figure 1: Genetic analysis identifying a homozygous likely pathogenic BLM splice-site variant (c.98+1G>T). Abbreviations: Chr: chromosome, HOM: homozygous

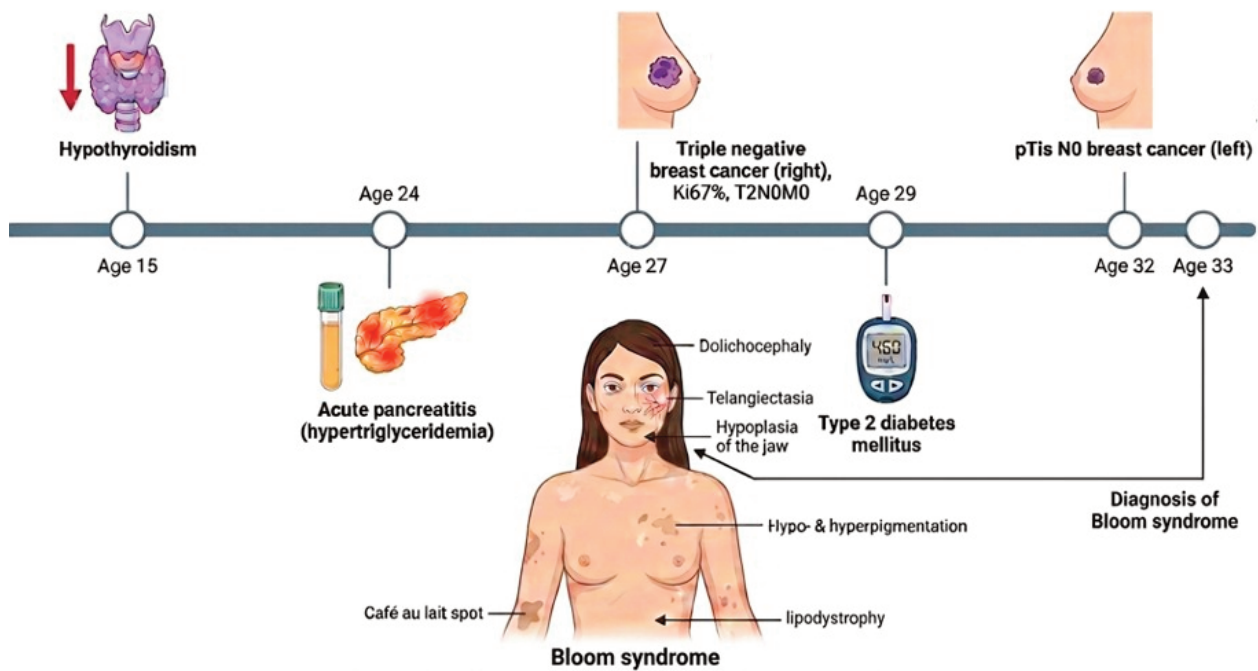


Figure 2: Clinical timeline of endocrine, metabolic, oncologic and genetic events (adapted from FigureLabs).

Laboratory Parameter	09/2022 (age 30)	Reference
HbA1c (%)	7.5	4-6%
HbA1c (IFCC, mmol/mol)	58	<42
C-peptide (nmol/L)	1.98	0.37-1.47
Glycaemia (mg/dL)	224	70-100
CRP (mg/dL)	1.7	<5
ALT (UI/L)	64	<33
AST (UI/L)	38	<32
ALP (UI/L)	64	35-104
Gamma GT (UI/L)	143	6-42
Lipase (U/L)	(pancreatitis diagnosis: 1 255)	23-300
Total cholesterol (mg/dL)	222 (pancreatitis diagnosis: 1 360)	<190
LDL cholesterol (mg/dL)	108	<100
Triglycerides (mg/dL)	364 (pancreatitis diagnosis: 12 356)	<175
TSH (mU/L)	2.66	0.27-4.2
Anti-TPO (kUI/L)	17	<34
CA 15-3 (kU/L)	27	<26

Figure 3: Table 1: Laboratory findings in the patient at age 30 and peak lipid levels at pancreatitis diagnosis

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Ovarian hyperstimulation syndrome and normal FSH?

Maybe not that normal!

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Abstract

Introduction

Pituitary neuroendocrine tumours (PitNETs), previously termed pituitary adenomas, are benign neoplasms arising from hormone-producing cells of the anterior pituitary gland. They are classified as functioning or non-functioning based on hormonal activity. Gonadotroph PitNETs originate from follicle-stimulating hormone (FSH)- and luteinizing hormone (LH)-secreting cells. They are typically clinically silent and therefore considered non-functioning. Rare functioning forms can occur and may cause precocious puberty in children, testicular enlargement in men, and menstrual irregularities, infertility, or ovarian hyperstimulation syndrome (OHSS) in premenopausal women [1]. OHSS presents with bilateral cystic enlargement of the ovaries, with a so-called “spoke-wheel” appearance on transvaginal ultrasound and is usually seen in patients receiving exogenous gonadotropin stimulation in the context of assisted reproductive technology [2]. When observed outside this context, a pituitary cause should be suspected, and FSH and LH levels measured.

Case report

A 36-year-old, gravida 2, para 2 woman with no significant medical history was referred to our tertiary centre for evaluation of bilateral enlarged polycystic ovaries. Initial biochemical evaluation while on combined oral contraceptives (OAC) showed a serum estradiol level of 1045 ng/L, LH of 0.42 U/L, and FSH of 6.31 U/L. After cessation of OAC, she developed oligomenorrhea, and the biochemical profile persisted. Initial external investigations, including adrenal imaging, were inconclusive. Moreover, an estradiol-secreting adrenocortical tumour would be expected to suppress gonadotropins and would not explain the ovarian enlargement.

Transvaginal ultrasound revealed massive bilateral ovarian enlargement with multilocular cystic morphology. The right and left ovaries were adjacent, measuring 77 × 103 × 99 mm and 80 × 85 × 78 mm, respectively. MRI of the pelvis confirmed the multilocular cystic lesions. The imaging findings resembled the characteristic appearance of OHSS; however, malignancy or a borderline lesion could not be excluded on imaging alone. A laparoscopic unilateral adnexectomy was undertaken to obtain a histopathological diagnosis. Pathological examination excluded malignancy and revealed multiple follicular cysts. Because of progressive ovarian enlargement and abdominal discomfort, treatment with the gonadotropin-releasing hormone (GnRH) antagonist linzagolix was initiated but discontinued after five months owing to a lack of clinical benefit.

Only after reassessment of the discordant hormonal profile was a central origin suspected. Pituitary MRI subsequently revealed a macroadenoma (14 × 19 × 17 mm) with suprasellar extension and invasion of the right cavernous sinus (Knosp grade 3a). Additional endocrine evaluation showed mild hyperprolactinemia (64.6 µg/L), presumably secondary to the hyperoestrogenaemia. No pituitary hormone deficiencies were identified.

Transsphenoidal resection of the tumour was performed, without perioperative or postoperative complications. Histopathology confirmed a PitNET, characterised by immunohistochemical expression of both FSH and LH. A rapid postoperative decline in estradiol levels, accompanied by normalisation of gonadotropins and prolactin, was observed within days, confirming the diagnosis of an FSH-secreting PitNET (Figure 1). Pituitary function was not affected, and clinical symptoms resolved.



Figure 1. Overview of longitudinal hormone measurements. Week 0 denotes the first visit at the referring centre. Reference ranges differed according to assay platform: Roche Cobas e601 (week -115), Siemens Atellica (weeks 0 and 10), and Roche Cobas 8000 (subsequent measurements).

Conclusion

Functioning gonadotroph PitNETs should be considered in women presenting with OHSS without fertility treatment. The key diagnostic clue is the combination of hyperoestrogenaemia and non-suppressed FSH and LH levels. Pituitary imaging should be part of the diagnostic work-up. Surgery is the treatment of choice, while gonadorelin analogues appear to have limited efficacy [3].

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Chorioretinal folds in severe Graves' orbitopathy: improvement after teprotumumab

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Abstract

Here we report the case of a male in his forties, non-smoker, followed in our hospital for severe thyroid eye disease. When he first consulted a clinician, he had biochemically proven Graves' hyperthyroidism and ophthalmologic examination showed active Graves orbitopathy (GO) with a clinical activity score (CAS) of 5/7 in the right eye and a CAS of 1/7 in the left. He was promptly started on thiamazole, β blockers, and selenium supplementation. In addition, intravenous methylprednisolone was administered according to the EUGOGO guidelines (1) for a cumulative dose of 4.5 grams. In the initial weeks of treatment, improvement was seen with a CAS of 3/7, but after 10 weeks – before the regimen was completed – refractory disease was noted with a marked increase in swelling and proptosis of the right eye, new onset metamorphopsia and visual loss. On further examination, a new finding of chorioretinal folds was observed on fundoscopy and confirmed on optical coherence tomography (OCT) (Figure 1 panel A-F). Chorioretinal folds appear “curtain”-like on fundoscopy and are a result of a change in the anatomical relationship between the sclera, the choroid and the retina. This rare entity has a varied etiology and is characterized by metamorphopsia and visual loss (2), which were present in our patient. Chorioretinal folds are a rare complication of Graves' orbitopathy, with only a limited number of reported cases. It is postulated that a combination of inflammation and choroidal venous congestion causes folding over Bruch's membrane(3). In the absence of diplopia, the patient preferred a deferral of orbital decompression. Second line medical treatment was sought out in favor of orbital decompression and teprotumumab (TEPEZZA®), a novel insulin-like growth factor I receptor (IGF-IR) inhibitor, was initiated because of the urgent clinical deterioration (4,5). Preliminary results after five injections spaced three weeks apart showed marked improvement in proptosis, CAS, metamorphopsia with regression of chorioretinal folds on fundoscopy and OCT (Figure 1 panel E-F). Therapy is well tolerated, with only mild hyperglycemia on the day of injection as a side effect. No hearing impairment was reported during treatment. This case highlights the efficacy and excellent tolerance of teprotumumab (TEPEZZA®) in treating a severe case of thyroid eye disease presenting with a rare complication of chorioretinal folds.

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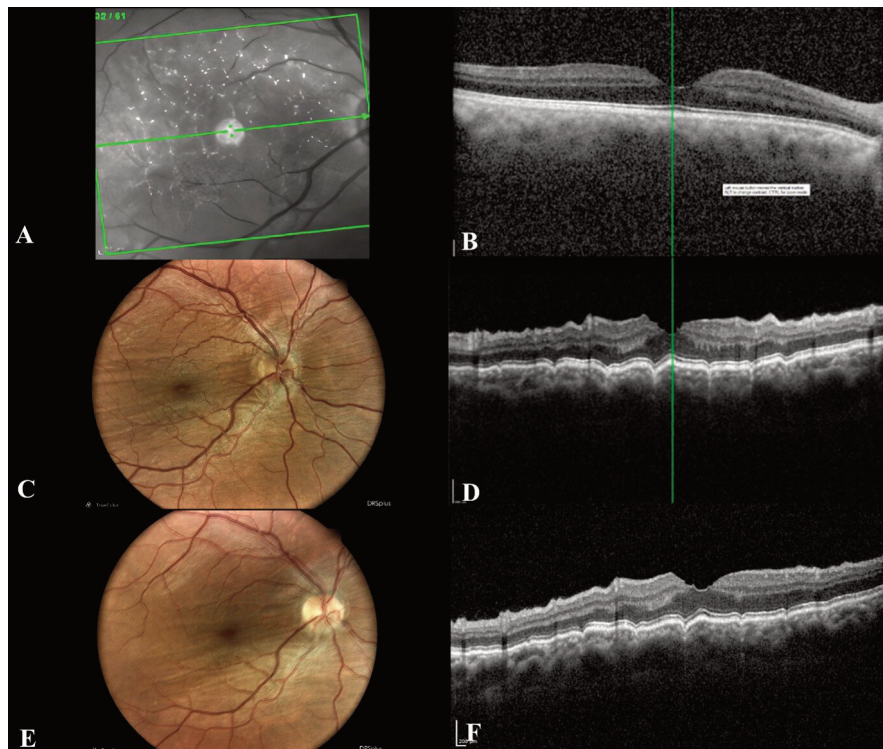


Figure 1. Appearance and later improvement of chorioretinal folds after initiating teprotumumab. A) Normal baseline funduscopy at diagnosis of Graves orbitopathy (GO). B) Normal OCT at baseline. C) Fundoscopy taken 10 weeks after initiating methylprednisolone treatment showing the curtain-like chorioretinal folds. D) Corresponding OCT. E) Fundoscopy showing improvement after the fifth dose of teprotumumab. F) Corresponding OCT, showing significant signs of improvement especially at the nerve fiber layer.

The silent catecholamine: a rapidly evolving, exclusively dopamine-secreting pheochromocytoma in a 22-year-old

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Abstract

Introduction

Pheochromocytoma and paraganglioma (PPGL) are rare neuroendocrine tumors, typically secreting norepinephrine and/or epinephrine. A distinct and uncommon variant is the dopamine-secreting PPGL, often presenting asymptotically, relatively large, and frequently extra-adrenal. Dopamine excess may independently indicate a higher malignancy risk.

Case report

We report the case of a 22-year-old man with an incidentally discovered right adrenal lesion. Biochemical evaluation revealed markedly elevated urinary dopamine and 3-methoxytyramine (3MT). Imaging showed a lipid-poor adrenal mass with minimal [18F]-fluorodeoxyglucose (FDG) avidity. Six months later, the lesion had significantly grown and increased in density, with further elevation of dopamine metabolites. The patient underwent robotic-assisted adrenalectomy following preoperative preparation with oral calcium channel blockers (CCB). Surgery was uneventful, and postoperative catecholamine levels normalized. Histopathology confirmed a pheochromocytoma without features of malignancy.

Conclusion

This case highlights the importance of age-specific management in individuals under 40 years, even when the lesion presents benign at first. Noncontrast computed tomography (CT) remains the initial imaging modality of choice. Standard treatment consists of surgical resection. In case of dopamine-excess in PPGL, CCB, rather than α -blockers, may be recommended for hemodynamic management.

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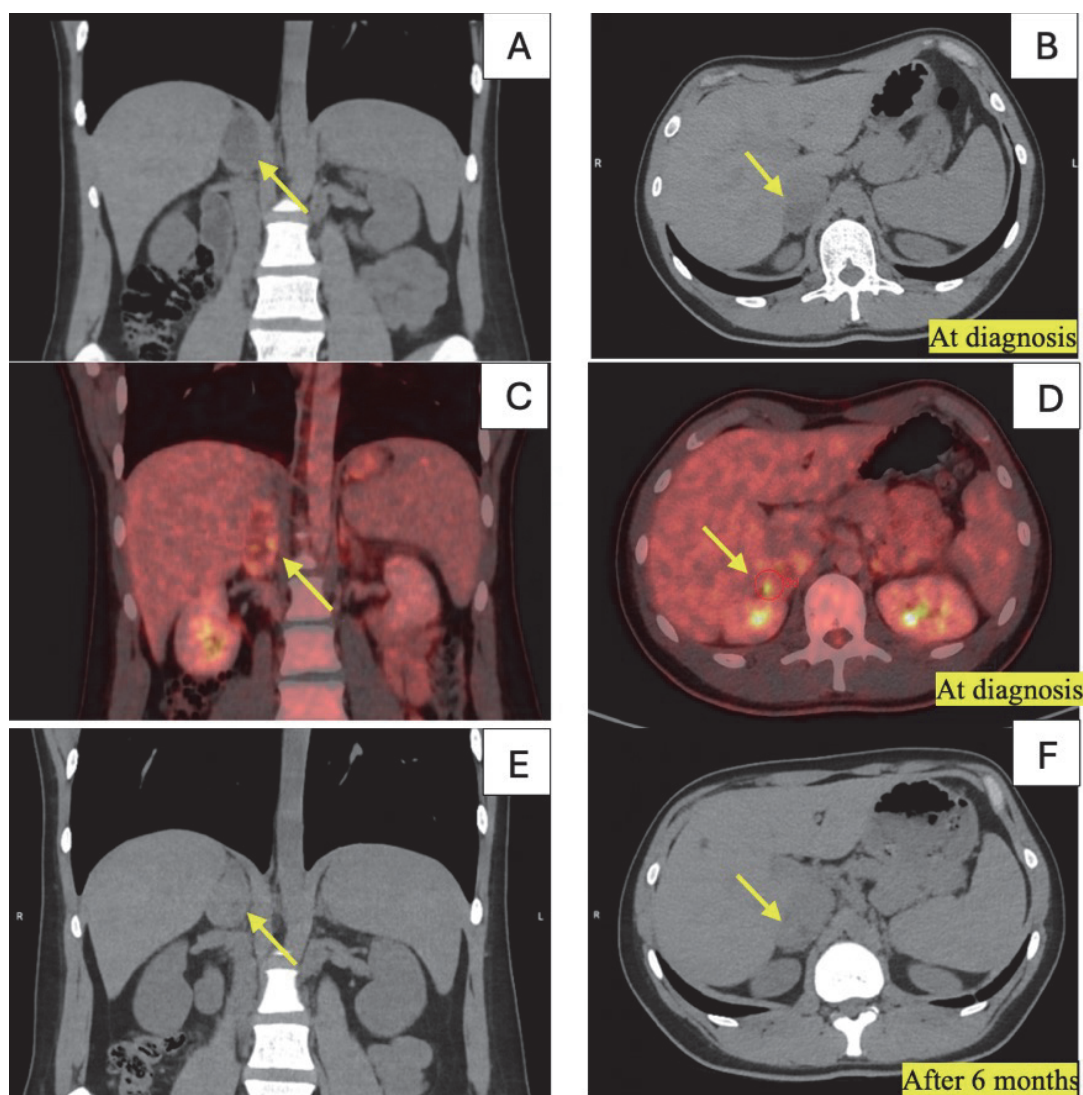


Figure 1. A full-dose unenhanced abdominal CT showed nodular transformation of the right adrenal gland, with dimensions of 3.5 x 2.1 x 4.6 cm and mean attenuation of 20 HU, consistent with a lipid-poor adrenal mass (A, B). 18F-FDG PET/CT revealed only minimal FDG avidity in the peripheral zone of the lesion (SUVmax 5.8), stable in size (C, D). Six months later, a follow-up CT revealed significant growth of the lesion with measurements reaching 4.2 x 2.3 x 4.6 cm and overall density up to 41 HU (E, F).

When hyponatremia deceives: isolated hypoaldosteronism as the first sign of autoimmune adrenal insufficiency

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Abstract

Introduction

Auto-immune adrenalitis is a rare condition affecting the adrenal cortex, often occurring within an auto-immune polyendocrinopathy. Although it usually presents with concurrent glucocorticoid and mineralocorticoid deficiency, we describe a case of isolated mineralocorticoid deficiency prior to global adrenal failure. Recognizing this atypical presentation is essential to guide timely hormone replacement and prevent clinical deterioration.

Case report

A 58-year-old woman presented at the emergency department with fatigue, dizziness, confusion, nausea and headache since 4 days. She was hemodynamically stable, afebrile, euvolemic and neurologically intact. Biochemistry demonstrated acute hypotonic hyponatremia (serum sodium 121 mmol/L, osmolality 261 mOsm/L) with concentrated urine (urine osmolality 669 mOsm/L, sodium 87 mmol/L, potassium 49 mmol/L, uric acid 41 mg/dL), normoglycemia, mild hyperkalemia (5.3 mmol/L), a slightly elevated serum creatinine to 1.1 mg/dL (baseline: 0.9–1.0 mg/dL), and low uric acid (2.3 mg/dL).

She had a background of type 1 diabetes mellitus managed with continuous subcutaneous insulin infusion (CSII, Medtronic 780G) complicated with nephropathy, retinopathy and hypoglycemia unawareness. Additionally, her history included autoimmune hypothyroidism, stage 1 sarcoidosis and a bifascicular block (right bundle branch block (RBBB) and left anterior hemiblock (LAHB)). At the time of presentation, the patient was treated with L-thyroxine, ezetimibe/rosuvastatin, fenofibrate and an ACE-inhibitor (perindopril).

Morning cortisol (12.4 µg/dL) and TSH (3.2 mIU/L) were within normal limits. She was admitted to the nephrology department where SIAD (syndrome of inappropriate antidiuretic hormone) was suspected given the patient's euvolemic status hyponatremia and concentrated urine. The ACE-inhibitor was discontinued, fluid restriction of 1L/day and 3g of sodium chloride tablets were started. To rule out malignancy, serum protein electrophoresis, free light chains, chest X-ray, abdominal ultrasound, mammography, and a PET-CT were performed, all were negative. Following treatment, despite high doses of sodium chloride, serum sodium improved but didn't normalize (132 mmol/L) and mild hyperkalemia persisted. Concurrently, clinical symptoms of confusion, lightheadedness, fatigue, and asthenia remained present.

Given the persistent hyperkalemia, the transtubular potassium gradient (TTKG) was assessed and found to be 4 (normal > 7), indicating mineralocorticoid deficiency. Endocrine workup confirmed hyperreninemic hypo-aldosteronism, demonstrating elevated ACTH of 272 pg/mL (ref: 7.2–63.3) and renin 1230 pg/mL (ref. supine: <35.7) alongside undetectable aldosterone <3.7 ng/dL (ref supine: 3.7–31.0). This biochemical pattern persisted after stopping the sodium chloride tablets. Initiating fludrocortisone 50µg twice daily resolved the hyponatremia. To investigate the underlying etiology, a differential diagnosis of auto-immune adrenalitis vs an enzymatic deficiency was considered. While the adrenal androgen panel was normal, testing for adrenal autoantibodies was positive, confirming an autoimmune etiology.

During follow-up symptoms of fatigue, myalgia and diarrhea persisted. Morning cortisol was slightly reduced at follow up to 6,4 µg/dL though it was taken at 11 a.m. Due to the high probability of progressive glucocorticoid failure, hydrocortisone replacement therapy of 10 mg in the morning was initiated, which led to a favorable clinical response.

Conclusion

This case highlights that adrenal insufficiency must be considered in the differential diagnosis of hypotonic hyponatremia, especially in patients with autoimmune polyendocrinopathies. Normal cortisol levels do not rule out adrenal disease, as isolated mineralocorticoid deficiency may occur first. Concurrent hyperkalemia and calculating the TTKG are simple tools that can help to uncover mineralocorticoid failure.



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