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Baseline clinical and treatment characteristics in a Dutch national cohort of patients with prolactinoma

Introduction

Current guidelines suggest that dopamine agonists (DAs) are the golden standard of treatment for prolactinoma patients. DAs do not *cure* the vast majority of prolactinoma patients, with post-withdrawal remission rates of approximately 34%. Therefore, many patients require prolonged DA treatment, while side effects negatively impact health-related quality of life (HR-QoL). Therefore, there is increasing interest in other treatment modalities, most importantly surgical tumor removal.

Prolactinoma studies

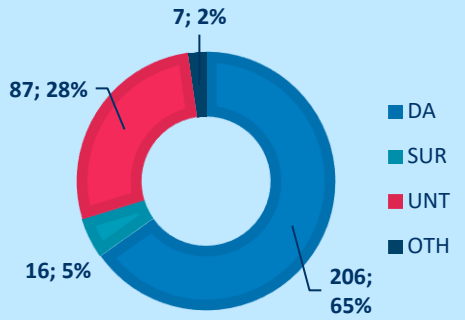
An innovative combined cohort randomized controlled trail design, starting with a national multicenter prospective cohort study (Prolac) aimed to map standard care for all prolactinoma patients, followed by an extensive detailed RCT study (PRolaCT) with an observational arm for patients with resectable prolactinomas, which aimed to compare DA treatment and surgery, was established.

Methods

Design At present, baseline clinical characteristics and available outcomes of the Prolac cohort study are presented. All clinical parameters were extracted from electronic patient files. Questionnaires regarding symptoms and adverse effects of increased prolactin levels and its respective treatment were filled out (PRO-CTCAE and HADS questionnaires).

Patients 325 prolactinoma patients were included (mean age 46.4±15.1 years; 210 female patients (64.6%)). Treatment data was available for 316 patients.

***Figure 1* Treatment modalities at inclusion** Data are shown as absolute numbers. DA, dopamine agonists; SUR, surgical treatment; UNT, untreated; OTH, other.



Characteristics at diagnosis

Mean age at diagnosis was 36.03±14.27 years. Assessed retrospectively, patients most frequently presented with or reported: libido loss (N=54/67, 80.6%), hypogonadism (N=143/191, 74.9%), galactorrhea (N=95/165, 57.6%), emotional complaints (N=38/44, 86.4%) and visual field loss (N=34/44, 77.3%). Median prolactin level was 106.10 µg/L (53.13 – 728.20, N=201). Patients were diagnosed with a microprolactinoma in 106/237 (44.7%) of cases.

Characteristics at inclusion

At inclusion, the majority of patients were treated at a tertiary care center (N=226, 69.5%). Median prolactin level was 19.70 µg/L (6.25 – 53.87, available for 229 patients), with 106 patients (46.3%) having serum prolactin levels above the gender-specific ULN.

***Table 1* Baseline characteristics of prolactinoma patients at inclusion** Data are shown as N and %. Prolactin levels available for 229 patients (males N=78, females N=151). Size available for 100 patients (males N=33, females N=67). Treatment data was available for 316 patients (males N=107, females N=209).

		All patients N=325	Males N=109 (33.5)	Females N=210 (64.6)	P-value
Age (years)		46.49 (± 15.10)	55.91 (± 15.79)	41.74 (± 12.21)	<0.001
Care at tertiary center		226 (69.5)	91 (83.5)	134 (63.8)	<0.001
Serum prolactin (µg/L)	Median (IQR)	19.70 (6.25 – 53.87)	11.75 (3.64 – 50.76)	22.56 (10.11 – 56.40)	0.006
	Prolactin above ULN	106 (46.3)	32 (41.0)	74 (49.0)	0.266
Prolactinoma size	Microprolactinoma	44 (44.0)	7 (21.2)	37 (55.2)	0.009
	Macroprolactinoma	30 (30.0)	16 (48.5)	14 (20.9)	
	Giant prolactinoma	1 (1.0)	0 (0.0)	1 (1.5)	
	No adenoma	13 (13.0)	4 (12.1)	9 (13.4)	
	Postoperative rest	12 (12.0)	6 (18.2)	6 (9.0)	
Treatment	Dopamine agonist	206 (65.2)	86 (80.4)	120 (57.4)	<0.001
	Surgery	16 (5.1)	5 (4.7)	11 (5.3)	
	No treatment	87 (27.5)	15 (14.0)	72 (34.4)	
	Other	7 (2.2)	1 (0.9)	6 (2.9)	

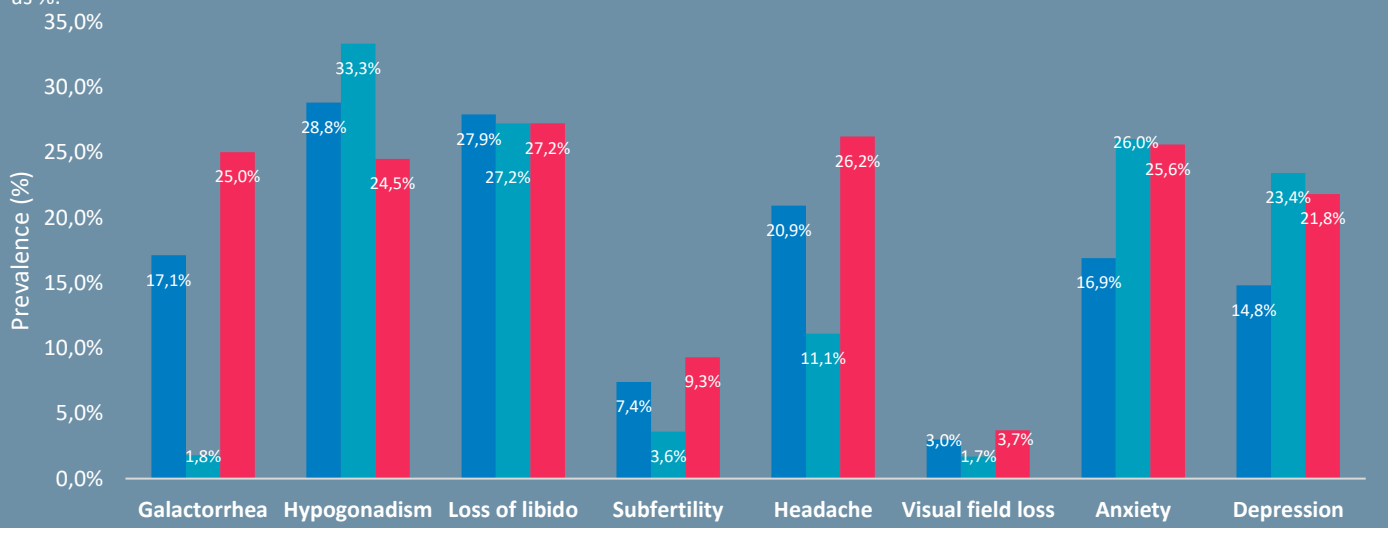
DA treatment

Mean age of DA-treated patients was higher than untreated patients (49.38± 15.41 vs 40.90±12.89 years, P<0.001), which was caused by the higher age of DA-treated male patients. Males and females were unequally divided over the treatment groups (females: DA-treated N=122 (58.1%); untreated N=87 (82.1%); males: DA-treated N=88 (41.9%) and untreated N=19 (17.9%), P<0.001). Untreated patients were more likely to have prolactin levels above the gender-specific ULN (N=52 (70.3%) *vs* N=54 (34.8%), P<0.001).

Symptoms and side effects

Despite being a cohort of (previously) treated patients, symptoms or side effects were reported at present. Hypogonadism (N=67/233, 28.8%), loss of libido (N=65/233, 27.9%), and headache (N=49/235, 20.9%) were frequently reported. Moreover, galactorrhea was present in 28/164 (17.1%) patients, whereas anxiety or depression disorder was present in 55 (16.9%) and 48 patients (14.8%), respectively. Male patients were more likely to report hypogonadism (males N=27/81 33.%; females N=36/147, 24.5%, P<0.001). Female patients more often reported galactorrhea (males N=1/56, 1.8%; females N=27/108, 25.0%, P<0.001), and headache (males N=9/81, 11.1%; females N=39/149, 26.2%, P=0.007).

***Figure 2* Presence of symptoms and side effects** Data are shown as %.



Are you inspired or interested?

We would like to thank all **primary investigators** and **participating centers** in the **Prolac** and **PRolaCT** studies. If you want more information, email us your questions about our research projects for patients with a prolactinoma via prolactinoom@lumc.nl.

Conclusions

In this Dutch national cohort of patients with prolactinomas, clinical characteristics at study inclusion are described, which is reflection of the present *real world* treatment effects. The present significant amount of reported symptoms or side effects have therefore occurred irrespective of treatment. Abnormal prolactin levels are observed frequently despite treatment. Moreover, sex differences in clinical and treatment characteristics were observed for virtually all parameters, suggesting the need for sex stratification in the future. Future projects should focus on the QoL of prolactinoma patients, and the potential role of surgery.

PRolaCT

Interested or participating centers
LUMC
AMC
VUmc
Radboud UMC
Maastricht UMC

ProlaC

Interested centers	Participating centers	
Dijklander Ziekenhuis	Alrijne Ziekenhuis	Amphia Ziekenhuis
Spaarne Gasthuis	St Antonius Ziekenhuis	Reinier de Graaf Gasthuis
Ysselland Ziekenhuis	AMC	Rijnstate Ziekenhuis
Maxima Medisch Centrum	VUmc	Radboud UMC
Rode Kruis Ziekenhuis	Gelre Ziekenhuis	Groene Hart Ziekenhuis
Albert Schweizer Ziekenhuis	Haaglanden Medisch Centrum	Isala Ziekenhuis
Elizabeth Twee Steden Ziekenhuis	LangeLand Ziekenhuis	Medisch Spectrum Twente
Deventer Ziekenhuis	Haga Ziekenhuis	UMCU
Flevo Ziekenhuis	Admiraal de Ruiter Ziekenhuis	UMCG
OLVG	Erasmus MC	LUMC
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