

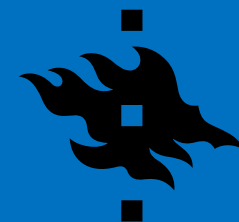
Effect of gender on symptoms at onset, diagnostic delay and response to thymectomy in patients with myasthenia gravis

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Background

- The role of gender on symptoms at onset, diagnostic delay and the prognosis of MG has not been extensively studied
- Onset symptoms and prognosis of MG:
 - One study showed no difference in the rate of achieving CSR between ocular or generalized onset symptoms for patients with eventually generalized MG [1]
- Diagnostic delay in MG:
 - Mean diagnostic delay was 2.1 years in a study of 1500 MG patients [2], where men had shorter delay than women (1.3 years vs 2.8 years)
 - Role in prognosis unclear
 - In small cohorts, short duration of preoperative symptoms has been associated with achieving remission after thymectomy [3,4,5]
 - In a study of 1002 patients, preoperative symptom duration was not related to remission [6]

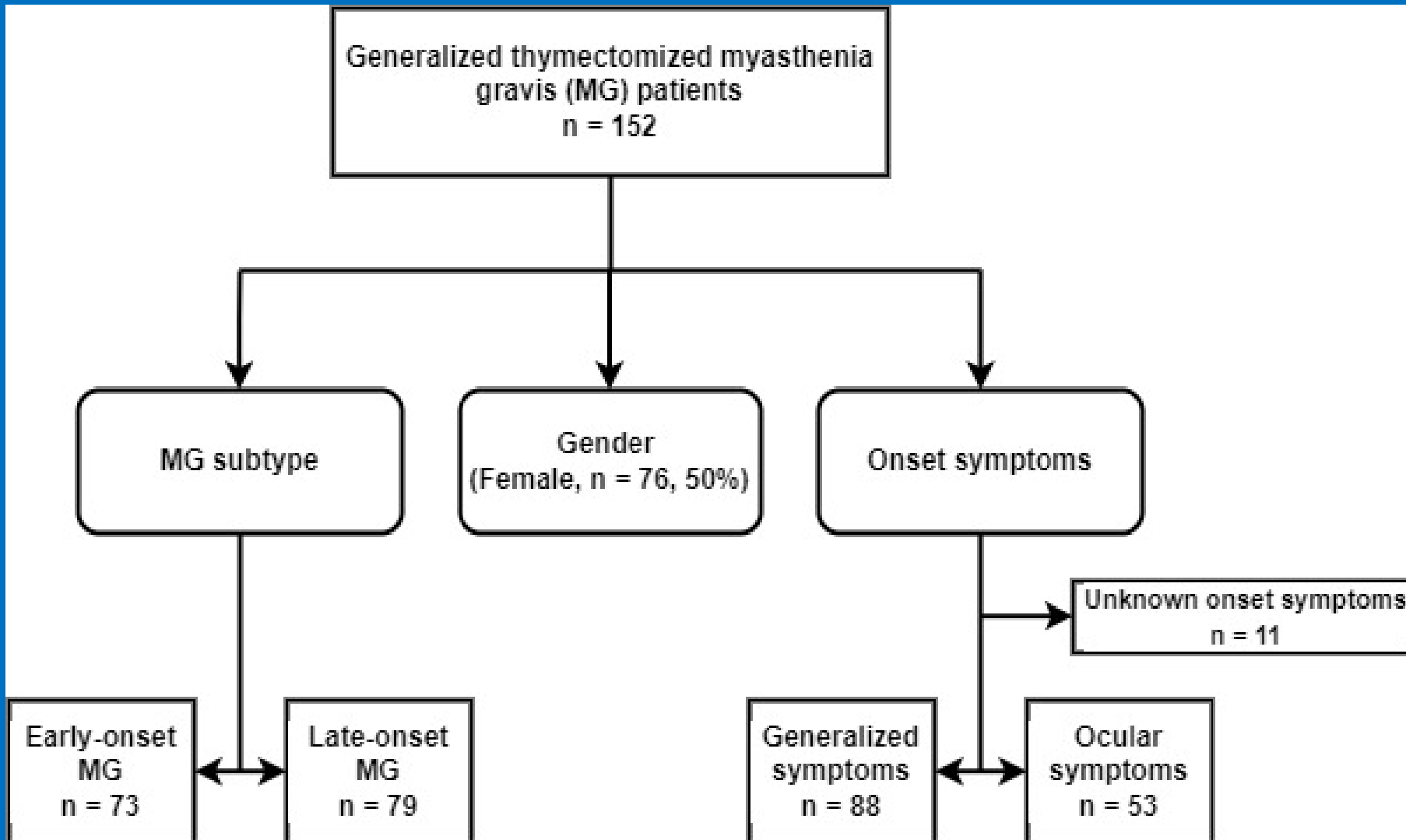
What is known about the effect of gender on prognosis of MG?

- Men with generalized MG have weaker proximal muscles than women and the muscle strength is not associated with disease duration or treatment intensity [7]
- Female gender is associated with a higher exacerbation rate [8]
- Women improve significantly less for all major clinical MG scales during 5-year follow-up [9]
 - The difference unaffected by disease duration, age, MG onset subtype (EOMG vs LOMG) or whether thymectomy has been performed

Methods

- Retrospective single-center cohort study
- 152 patients with generalized MG who underwent a thymectomy between 1999 to 2015 in Helsinki University Hospital
- The patients were followed from the diagnosis of MG until their last visit at the neurology outpatient clinic
- Follow-up data from the hospital medical records
- Outcome measures:
 - Pyridostigmine dose at the last follow-up visit
 - Complete stable remission (CSR; no medications for at least 1 year before last visit)
 - Minimal need of medication
 - Postoperatively used pyridostigmine as only MG medication (max 100 mg per day) or achieved CSR
 - Need for in-hospital treatments
 - Requiring treatment at ICU or receiving high-dose IV methylprednisolone, plasma exchange or IV immunoglobulin for exacerbations during the post-thymectomy follow-up period

Illustration of the study cohort



- 84.2 % AChR-ab+
- Mean age at diagnosis was 48.7 (± 16.9) years
- Mean follow-up time 8.8 (± 5.1) years post-thymectomy
- AChR-ab status, preoperative MGFA classification and delay from diagnosis to thymectomy similar for men and women; women younger at diagnosis (37.8y vs 56.7y)

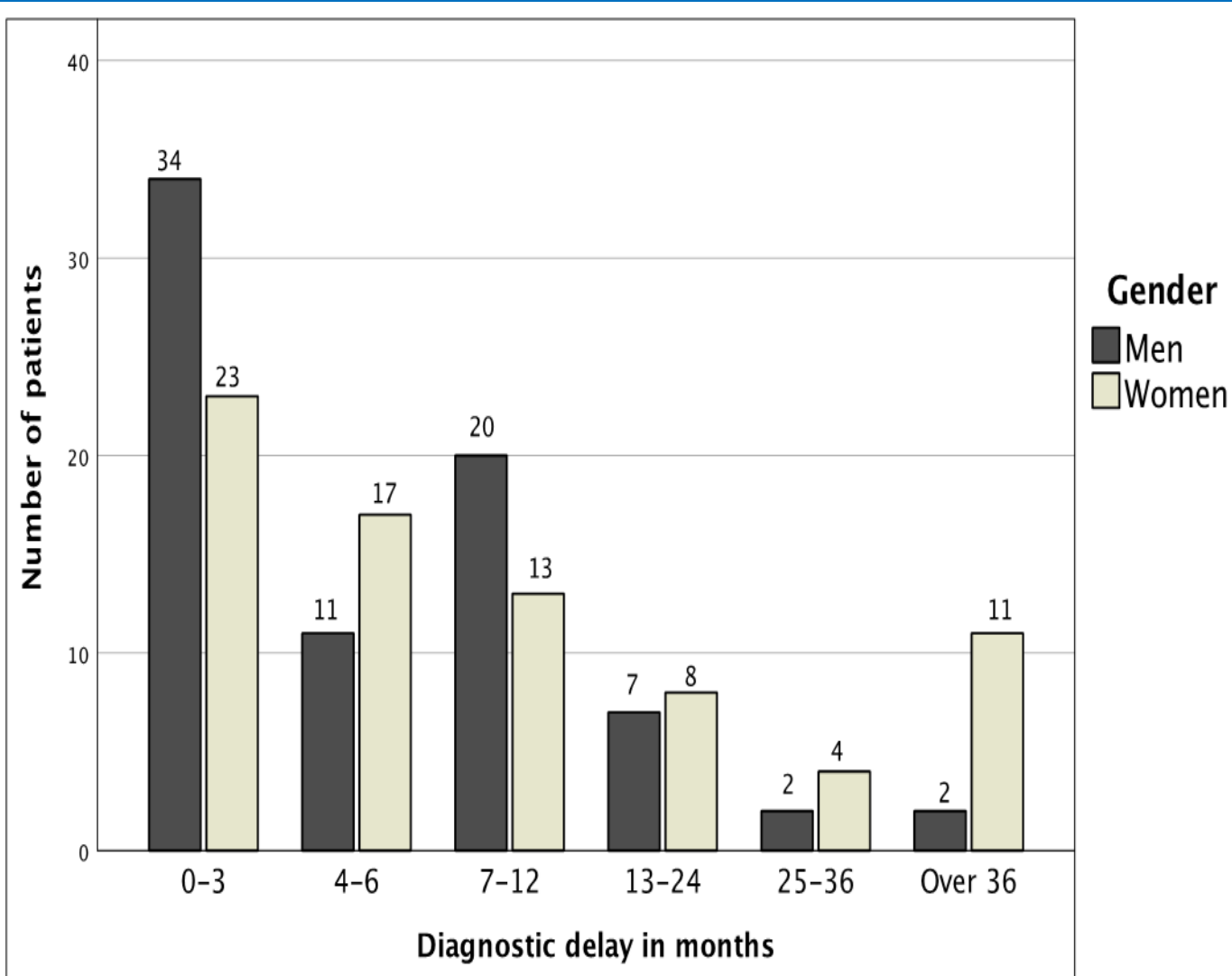
Main results of the study

Symptoms at disease onset differ between female and male patients

Type of symptoms at onset	All	Women	Men	P-value
Ocular, n (%)	53 (34.9%)	16 (21.1%)	37 (48.7%)	0.001
Generalized, n (%)	88 (54.6%)	54 (71.1%)	34 (44.7%)	0.002
Unknown, n (%)	11 (7.2%)	6 (7.9%)	5 (6.6%)	NS

- Ocular onset symptoms more frequent for men
- Generalized onset symptoms more frequent for women
- No correlation was found between type of onset symptoms and the length of diagnostic delay

Female MG patients have a longer diagnostic delay



- Median diagnostic delay of 5.5 (range 0 - 117) months
 - Longer for women than men (median 6.2 months [range 0-117] vs 4.9 months [range 0.1 - 83.7] respectively; $P = 0.018$)
- Diagnostic delay under 12 months was more common in men
 - 69.7 % of female patients vs 85.5 % of male, $P = 0.031$
- Diagnostic delay over 24 months was more common in women
 - 19.7 % of female patients vs 5.3% of male, $P = 0.013$

Effect of gender on the symptoms at onset and diagnostic delay in EOMG and LOMG subtypes

	Women with EOMG	Men with EOMG	P-value	Women with LOMG	Men with LOMG	P-value
N	57	16		19	60	
Diagnostic delay, median (range) in months	5.96 (0–94.9)	5.76 (31.2–0.3)	NS	6.5 (0.7–117.5)	4.65 (0.1–83.7)	0.004
Ocular symptoms at onset, n (%)	12 (21.1%)	7 (43.8%)	NS	4 (21.1%)	30 (50.0%)	0.034
Generalized symptoms at onset, n (%)	42 (73.7%)	6 (37.5%)	0.015	12 (63.2%)	28 (46.7%)	NS

- Diagnostic delay was longer for women than for men with LOMG
- Ocular symptoms at onset were more frequent for men than for women with LOMG
- Generalized symptoms at onset were more frequent for women than for men with EOMG

Response to thymectomy correlates to age at onset

- 20 patients (13.2%) achieved CSR
 - More common in EOMG patients as compared to LOMG patients, 20.5% vs 6.3%, P = 0.031
- Younger age increased the likelihood of reaching CSR (P = 0.014, binary logistic regression)
 - No effect: gender, diagnostic delay or presenting onset symptoms of MG

	OR	95% CI	P-value
Gender (men)	0.85	0.22 - 3.39	NS
Diagnostic delay	1.02	0.99 - 1.04	NS
Type of symptoms at onset	1.57	0.50 - 4.87	NS
Age at onset of symptoms	0.95	0.92 - 0.99	0.014*

OR, odds ratio; CI, confidence interval; NS, non-significant . *Statistically significant at the P < 0.05 level

Response to thymectomy correlates to the age at onset but not to gender, diagnostic delay or presenting symptoms

- No gender differences regarding the rate of CSR, mean pyridostigmine dose at the last follow-up or need for in-hospital treatments
 - Remained unchanged when we further divided the men and women into EOMG and LOMG subgroups
- The higher the age at onset the more likely the need for in-hospital treatments for exacerbations of MG
 - OR 1.05, 95%, CI: 1.02-1.07, P = 0.002
- No significant differences in outcome measures at the last follow-up visit among diagnostic delay subgroups (<12 months, 12-24 months, >24 months)

Response to thymectomy in relation to symptoms at the onset of eventually generalized MG

	Ocular symptoms	Generalized symptoms	P-value
Number of patients	54	88	-
CSR at the last follow-up visit, n (%)	8 (14.8%)	11 (12.5%)	NS
Minimal need of medication at the last follow-up visit, n (%)	11 (20.4%)	18 (20.5)	NS
Need for in-hospital treatments, n (%)	24 (44.4%)	34(38.6%)	NS
Immunosuppressive drugs at last follow-up visit, n (%)	18 (33.3%)	32 (36.4%)	NS
Pyridostigmine dose at the last follow-up visit, mg, mean (±SD)	182.3 (±104.9)	240.5 (±152.8)	0.025

Conclusions

- Our results reinforce the current consensus guidelines of treatment of MG that thymectomy should be considered based on age at diagnosis in generalized MG patients [10]
 - Longer diagnostic delay should not cause hesitation
- In addition to the differences in the typical age at onset of MG between men and women, there seem to be gender-related differences in the disease course
 - More studies are needed in the future

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