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ORIGINAL ARTICLE

Dysphagia increases the risk of post-stroke fatigue

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Abstract

Background: Post-stroke dysphagia is known to have a pronounced effect on mortality and quality of life of stroke patients. Here, we investigate whether this extends to post-stroke fatigue, a major contributor to morbidity after ischemic stroke.

Methods: Patients with acute ischemic stroke (recruited consecutively in the STROKE-CARD Registry from 2020 to 2023 at the study center Innsbruck, Austria) were examined for dysphagia via clinical swallowing examination at hospital admission. Post-stroke fatigue was assessed using the Fatigue Severity Scale (FSS) at study specific in person follow-up visits within the first year after ischemic stroke.

Results: Among 882 ischemic stroke patients (mean age 72.4 ± 13.5 years, 36.8% females), dysphagia was present in 22.0% at hospital admission and persisted in 16.2% until hospital discharge. Post-stroke fatigue affected 52.2% of the total cohort during follow-up and was significantly more prevalent among those with dysphagia (68.4% vs. 49.0%, $p < 0.001$). The prevalence of fatigue increased with the severity of dysphagia, with the highest proportion (86.7%) in those with severe dysphagia. After multivariable adjustment for other factors associated with post-stroke fatigue, including age, sex, pre-stroke disability, cognitive impairment, stroke severity, inability to walk at discharge, and need for antidepressants at discharge, dysphagia remained independently associated with post-stroke fatigue during the first year after stroke (odds ratio [OR]: 2.03, 95% confidence interval [CI]: 1.22–3.38).

Conclusions: Dysphagia is common after ischemic stroke and increases the risk of post-stroke fatigue. Patient-tailored measures are warranted to reduce fatigue after stroke and therefore enhance quality of life.

KEYWORDS
dysphagia, fatigue, ischemic stroke

The STROKE-CARD registry study group: Gregor Broessner, Julia Ferrari, Julian Granna, Ton Hanel, Katharina Kaltseis, Theresa Köhler, Stefan Krebs, Florian Krismer, Christoph Mueller, Wolfgang Nachbauer, Anna Neuner, Anja Perfler, and Christine Span.

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INTRODUCTION

Stroke remains one of the main contributors of global mortality. It also entails numerous complications in survivors leading to long-term morbidity [1, 2]. Dysphagia, being the inability to swallow, is one such frequent post-stroke complication. It affects 21%–32% of stroke patients in the aftermath and is accompanied by reduced quality of life and increased short-term mortality [3–8]. Prior investigations have also linked dysphagia to psychosocial sequelae such as social isolation, anxiety, and depression, indicating a particular burden in everyday life of stroke survivors [5, 9, 10]. One psychosocial consequence of stroke and its association to dysphagia has previously been neglected: Nearly 50% of all stroke survivors develop post-stroke fatigue, which is considered to be a subjective feeling of mental and/or physical weakness or exhaustion not mitigated by rest [11, 12]. Post-stroke fatigue is also known to increase mortality and represents a particular challenge in neurological rehabilitation, as therapeutic approaches are still lacking [13, 14].

AIMS AND HYPOTHESIS

In this study, we investigate the prevalence of and potential link between post-stroke fatigue and post-stroke dysphagia in ischemic stroke survivors.

METHODS

Study population

Within the prospective STROKE-CARD Registry (NCT04582825), consecutive patients (age ≥ 18 years) with acute ischemic stroke and high-risk transient ischemic attack (TIA; $ABCD_2$ score ≥4) were recruited. The STROKE-CARD Registry was initiated after the successful conclusion of the STROKE-CARD trial (2014–2019; NCT02156778), a post-stroke disease management program now implemented as standard of care in participating centers (Medical University of Innsbruck, Hospital St. John's of God Vienna) [15]. The STROKE-CARD Registry adheres to the trial's protocols, which encompass a standardized and comprehensive clinical status as well as risk factor assessment at the index event, which is carried out at a 3- and 12-month post-stroke in-person follow-up visit with stroke experts. During follow-up, treating stroke physicians focus on individualized treatment modifications concerning risk factor control as well as screening for post-stroke complications and post-stroke deficits.

For this analysis, all ischemic stroke patients recruited at the Medical University of Innsbruck from December 2020 to January 2023 were included.

The local ethics committee of the Medical University of Innsbruck approved the STROKE-CARD Registry study (1182/2020). All patients gave informed consent.

Study measures

Detailed study procedures and variables recorded within the STROKE-CARD Registry can be found elsewhere (NCT04582825) [10, 16].

As part of STROKE-CARD standard of practice, all patients were screened for potential swallowing difficulties upon admission. Dysphagia was diagnosed through clinical swallowing examination conducted by speech and language therapists. If necessary, this assessment was complemented by additional diagnostic procedures such as fiberoptic endoscopic evaluation of swallowing. Dysphagia severity was categorized according to the recorded nutritional recommendations into mild (prohibition of mixed consistencies), moderate (prohibition of liquids without thickening), and severe (no oral nutrition). Dysphagia persistence until hospital discharge was defined as no return to total oral feeding with further requirement for speech therapy.

Further key variables included within this analysis were pre-stroke and post-stroke functional status, measured by modified Rankin Scale (mRS), stroke severity at onset, applying the National Institute of Health Stroke Severity Scale (NIHSS), evidence of cognitive impairment, documented in clinical records, and antidepressant intake at discharge [17–19]. The following were considered as antidepressant agents: tetracyclics, selective serotonin reuptake inhibitors, selective and non-selective serotonin–norepinephrine reuptake inhibitors, noradrenergic, and specific serotonergic antidepressants.

Post-stroke fatigue was recorded during study specific in-person follow-up visits, at 3 and 12 months post stroke, using the validated Fatigue Severity Scale (FSS) [20, 21]. The FSS is a self-report questionnaire including nine items, each item graded from 1 (strong disagreement) to 7 (strong agreement). The mean value of the nine items implicates the final score with a score of ≥4 being considered as presence of fatigue [20, 21].

Statistical analysis

Patient characteristics are demonstrated as mean ± standard deviation (SD), median (interquartile range [IQR]) or count (percentage). Comparative analyses were performed on groups of patients, with or without dysphagia, utilizing Mann–Whitney *U*-tests for continuous variables and Pearson's chi-squared tests for categorical variables. None of the continuous variables were normally distributed (assessed by Shapiro–Wilk tests). Bonferroni adjustment accounted for multiple testing in univariate comparisons, and missing data are presented in the tables. The independent association between dysphagia and fatigue was assessed using logistic regression. Three models were used: adjustment for age, sex and date of questionnaire completion (model 1), additional adjustment for NIHSS at admission and pre-stroke mRS (model 2), and additional adjustment for inability to walk at discharge, need for antidepressants at discharge and cognitive impairment (model 3). A significance level of 0.05 was applied. The statistical analyses were

conducted using SPSS Version 27.0.1.0 (IBM Corporation, Armonk, New York).

RESULTS

The cohort comprises 882 ischemic stroke patients (Figure 1). Table 1 presents key features of the entire cohort, and the subgroups analyzed.

In short, 194 of 882 (22.0%) had post-stroke dysphagia at hospital admission, with 41.2% being considered as mild, 45.6% as moderate, and 13.2% as severe. Patients with post-stroke dysphagia were older ($p < 0.001$), more likely to have cognitive impairment ($p = 0.004$) and had a greater pre-stroke disability as indicated by the pre-stroke mRS ($p < 0.001$) compared to stroke patients without stroke. In addition, patients with post-stroke dysphagia were more likely to have right-sided lesions and anterior circulation strokes (both $p < 0.001$), higher stroke severity as indicated by NIHSS ($p < 0.001$), and were more likely to be unable to walk at hospital discharge ($p < 0.001$). Furthermore, patients with post-stroke dysphagia were more likely to be prescribed antidepressants at discharge ($p < 0.001$). Dysphagia persisted until hospital discharge in 143 patients, accounting for 73.2% of those with initial dysphagia and 16.2% of the total cohort.

Concerning post-stroke fatigue, FSS questionnaires were available in 78.9% of post-stroke survivors, with 78.2% being collected within the first 6 months post-stroke and 21.8% being obtained

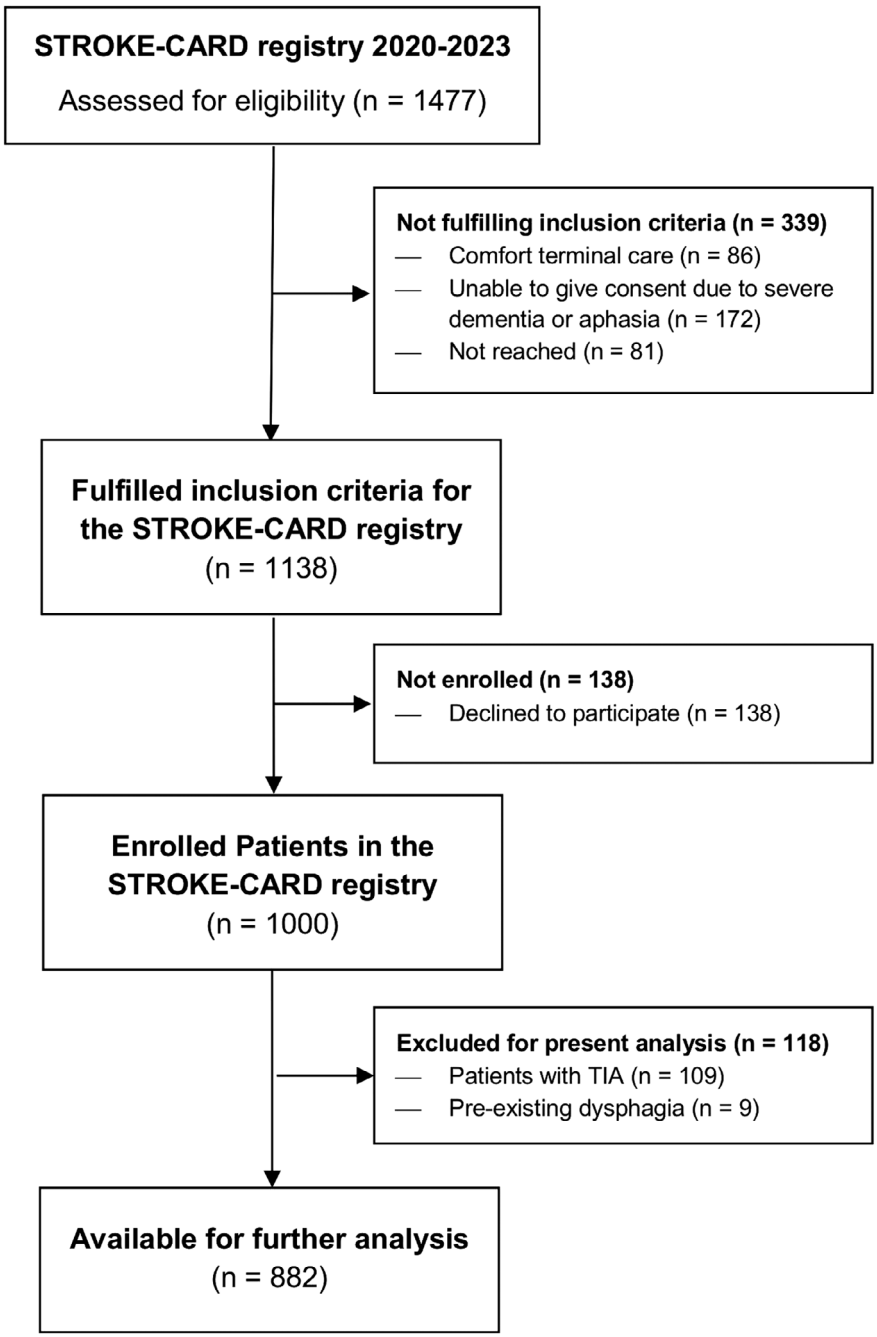

FIGURE 1 Study flowchart.

TABLE 1 Baseline characteristics.

	All patients ($n=882$)	Dysphagia ($n=194$)	No dysphagia ($n=688$)	
	n (%), mean ± SD, median (IQR)			p-value*
Baseline characteristics				
Female sex	325 (36.8%)	73 (37.6%)	252 (36.6%)	0.799
Age (in years)	72.4 ± 13.5	75.7 ± 12.2	71.5 ± 13.7	<0.001
Cognitive impairment	36 (4.1%)	15 (7.7%)	21 (3.1%)	0.004
Pre-stroke mRS	0 (0–0)	0 (0–1)	0 (0–0)	<0.001
Index event				
Stroke territory				
Anterior circulation	537 (60.9%)	142 (73.2%)	395 (57.4%)	<0.001
Posterior circulation	234 (26.5%)	27 (13.9%)	207 (30.1%)	<0.001
Both	111 (12.6%)	25 (12.9%)	86 (12.5%)	0.886
Lesion localization				
Unilateral left	400 (45.4%)	66 (34.0%)	334 (48.5%)	<0.001
Unilateral right	365 (41.4%)	103 (53.1%)	262 (38.1%)	<0.001
Bilateral lesion	117 (13.3%)	25 (12.9%)	92 (13.4%)	0.860
Outcome measures				
NIHSS at admission	2 (1–5)	7 (4–14)	2 (1–4)	<0.001
Inability to walk at discharge[a]	104 (11.8%)	64 (33.0%)	40 (5.8%)	<0.001
Discharged on antidepressants	145 (16.4%)	64 (33.0%)	81 (11.8%)	<0.001

[a]Defined as modified Rankin Scale ≥4.

*Adjusted for multiple testing (Bonferroni method), $p \leq 0.003$ can be considered significant.

between 6 and 12 months post-stroke. A total of 52.2% of individuals assessed had a mean FSS score ≥4, therefore being diagnosed with post-stroke fatigue. Patients with post-stroke dysphagia had a significantly higher proportion of post-stroke fatigue than those without swallowing impairment ($p<0.001$). Furthermore, the prevalence of post-stroke fatigue increased nominally with the severity of post-stroke dysphagia, with the highest proportion (86.7%) in those with severe dysphagia ($p<0.001$; Figure 2).

Table 2 demonstrates the independent association between dysphagia and fatigue applying several models. Even after adjustment for age, sex, pre-stroke mRS, NIHSS at admission, cognitive impairment, inability to walk at discharge and need for antidepressants at discharge, and dysphagia, evident both at hospital admission and persisting at discharge, was independently associated with fatigue (dysphagia at admission: OR: 2.03, 95% CI: 1.22–3.38; dysphagia at discharge: OR: 1.98, 95% CI: 1.12–3.48). Inclusion of stroke localization (territory and lesion side) yielded the same results (data not shown).

DISCUSSION

Fatigue affects one out of two stroke survivors, which is consistent with our findings [13, 22]. Various studies have shown an association between post-stroke fatigue and female sex, increasing age, pre-stroke fatigue, cognitive impairment, a higher degree of disability and depressive symptomatology [22–25]. Our results demonstrate a strong association between post-stroke dysphagia and fatigue independent of these factors (Figure 2 and Table 2).

The inability to swallow is known to be related to social withdrawal and loss of joy [9]. While most patients recover from dysphagia within a short period of time after a stroke, recent research has revealed that there may be subsequent psychological sequelae, potentially leading to chronic symptoms of depression and anxiety [10, 26]. Our current analysis extends the negative impact of stroke-related dysphagia on life after stroke by emphasizing on its association with post-stroke fatigue, which is known to impair post-stroke quality of life and rehabilitation [27–30]. A recent meta-analysis has shown that post-stroke fatigue leads to an increased need for care and less independence in daily activities, resulting in lower quality of life, especially within the first 6 months after stroke [30]. However, post-stroke fatigue goes beyond intraindividual effects and has socioeconomic effects as stroke survivors suffering from fatigue are less likely to return to work or, if they do, are more likely to have functional limitations and poor decision-making control, which in turn may hamper efficiency [31, 32].

The underlying causes of the potential connection between dysphagia and fatigue, as well as depression, remain unclear. Dysphagia

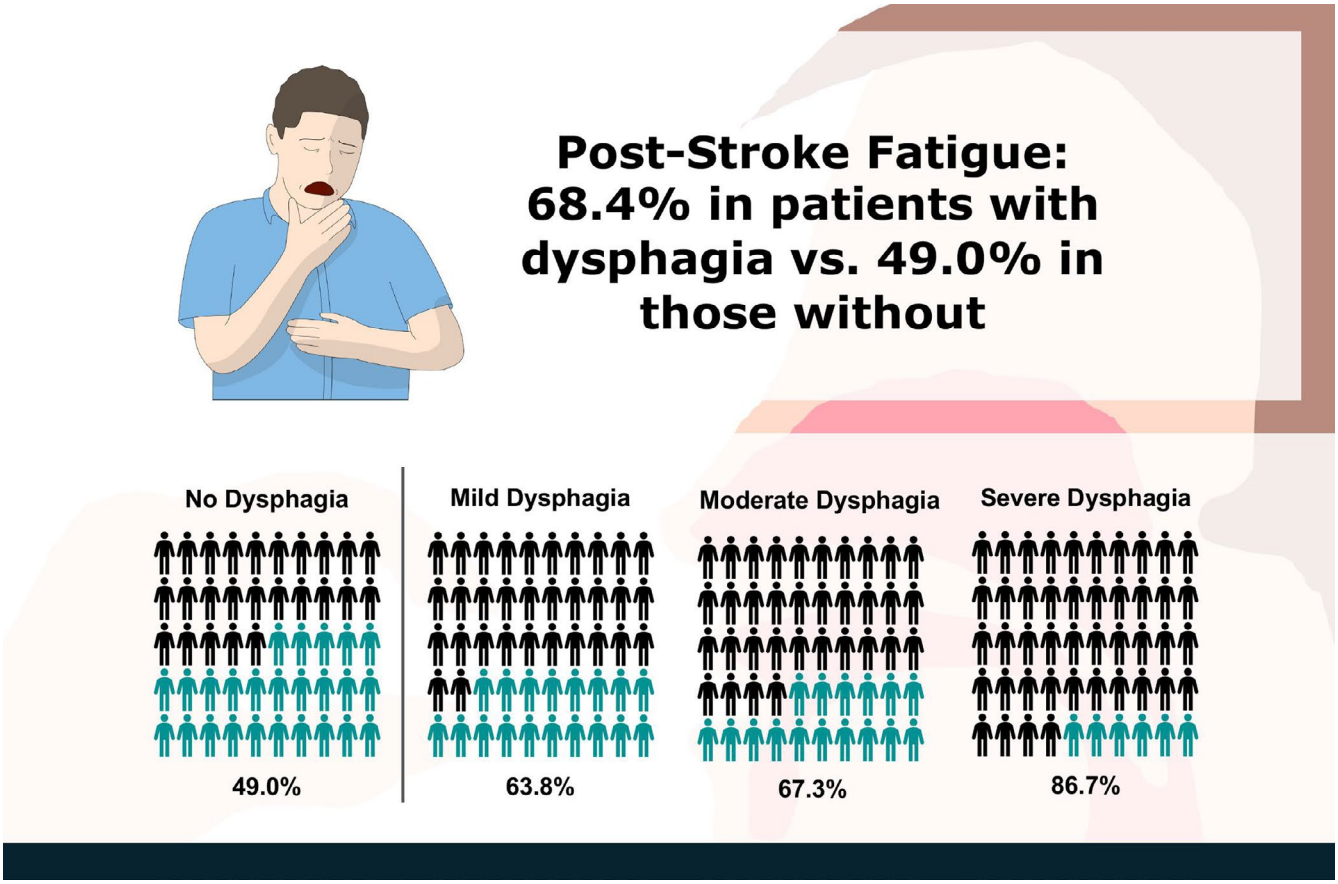

FIGURE 2 Proportion of post-stroke fatigue in patients with dysphagia after stroke.

TABLE 2 Association between post-stroke dysphagia and post-stroke fatigue.

	No dysphagia at admission ($n = 582$)	Dysphagia at admission ($n = 114$)		No dysphagia at discharge ($n = 609$)	Dysphagia at discharge ($n = 87$)	
	Prevalence (%)		*p*-value	Prevalence (%)		*p*-value
Univariable						
Fatigue (FSS ≥4)	337 (49.0%)	133 (68.4%)	<0.001	302 (49.6%)	61 (70.1%)	<0.001
	No dysphagia at admission ($n = 582$)	**Dysphagia at admission ($n = 114$)**		**No dysphagia at discharge ($n = 609$)**	**Dysphagia at discharge ($n = 87$)**	
	Odds ratio (95% CI)		***p*-value**	**Odds ratio (95% CI)**		***p*-value**
Multivariable						
Model 1	1.00 [ref.]	2.24 [1.45, 3.44]	<0.001	1.00 [ref.]	2.36 [1.44, 3.85]	<0.001
Model 2	1.00 [ref.]	2.28 [1.40, 3.72]	0.001	1.00 [ref.]	2.23 [1.31, 3.81]	0.003
Model 3	1.00 [ref.]	2.03 [1.22, 3.38]	0.006	1.00 [ref.]	1.98 [1.12, 3.48]	0.018

Note: Odds ratios for the association between post-stroke fatigue and dysphagia at hospital admission and discharge. Model 1: Adjustment for age, sex, and date of questionnaire completion. Model 2: Model 1, pre-stroke mRS and NIHSS at admission. Model 3: Model 2, cognitive impairment, inability to walk (mRS ≥4) at discharge, and need for antidepressants at discharge.

Abbreviations: CI, confidence interval; FSS, Fatigue Severity Scale; mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale; OR, odds ratio.

results in malnutrition and poor sleep quality, both of which are common after stroke and are associated with fatigue and depression [33–40]. Moreover, on a neuronal level, the onset of both fatigue and dysphagia after stroke has been linked to ischemic lesions in the basal ganglia and thalamus [41–45]. However, these assumptions remain hypothetical.

Although our data show a clear association between post-stroke dysphagia and post-stroke fatigue, it is unclear whether appropriate

treatment and management of dysphagia would have a positive impact on fatigue symptoms. With few small studies and one case report indicating a possible improvement in fatigue symptoms in patients with intensified dysphagia treatment compared with standard treatment, this hypothesis warrants future investigation [46–49].

The strength of our study is our large cohort of consecutive, unselected ischemic stroke patients with standardized assessment of post-stroke dysphagia as well as post-stroke fatigue, resulting in a representative prevalence of both post-stroke fatigue and post-stroke dysphagia within this cohort compared with the literature. We utilized a validated screening tool for fatigue, which was available in over three quarters of patients within the first year. Prior studies were limited by the lack of a standardized dysphagia assessment, which relied solely on patient-reported swallowing difficulties, and the prevalence of fatigue in patients with dysphagia at stroke onset neglecting intraindividual follow-up [50].

Limitations include the use of the tissue-based definition of stroke, which may result in a slight propensity for milder strokes in our cohort, and the fact that despite the overall low rate of loss to follow-up, fatigue questionnaires were missing in a moderate proportion of patients. Furthermore, this cohort consists of >99% patients from European descent; therefore, our results cannot be generalized to more ethnically diverse populations and regions. Finally, we had no available data on malnutrition to investigate the effect on fatigue in our cohort.

CONCLUSION

Stroke-related dysphagia is an independent factor for developing post-stroke fatigue, a post-stroke complication which is difficult to treat and a major contributor to morbidity after stroke. An intensified dysphagia diagnosis and therapy concept may be beneficial in preventing post-stroke fatigue to ameliorate quality of life in stroke survivors, and therefore warrants further studies.

AUTHOR CONTRIBUTIONS

Anel Karisik: Conceptualization; investigation; funding acquisition; writing – original draft; methodology; validation; visualization; writing – review and editing; formal analysis; software; project administration; data curation; supervision; resources. **Kurt Moelgg:** Writing – review and editing; formal analysis; data curation. **Lucie Buergi:** Writing – review and editing; formal analysis; data curation. **Lukas Scherer:** Writing – review and editing; formal analysis; data curation. **Theresa Schneider:** Writing – review and editing; formal analysis; data curation. **Benjamin Dejakum:** Writing – review and editing; formal analysis; data curation. **Silvia Komarek:** Writing – review and editing; formal analysis; data curation. **Christian Boehme:** Writing – review and editing; formal analysis; data curation; supervision; project administration. **Thomas Toell:** Writing – review and editing; formal analysis; supervision; data curation. **Raimund Pechlaner:** Writing – review and editing; formal analysis; supervision; data curation. **Simon Sollereder:** Writing – review and editing; formal analysis; supervision. **Sonja Rossi:** Writing – review and editing; formal analysis; supervision. **Michael Thomas Eller:** Writing – review and editing; data curation; formal analysis. **Gudrun Schoenherr:** Data curation; supervision; formal analysis; writing – review and editing. **Wilfried Lang:** Writing – review and editing; project administration; formal analysis; supervision. **Stefan Kiechl:** Writing – review and editing; validation; formal analysis; project administration; supervision; funding acquisition; conceptualization; investigation. **Michael Knoflach:** Funding acquisition; investigation; conceptualization; validation; writing – review and editing; formal analysis; project administration; supervision. **Lukas Mayer-Suess:** Investigation; conceptualization; funding acquisition; writing – original draft; writing – review and editing; visualization; validation; methodology; software; project administration; formal analysis; resources; supervision; data curation.

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CONFLICT OF INTEREST STATEMENT

None of the authors report disclosures relevant to this research.

DATA AVAILABILITY STATEMENT

Anonymized patient data are available for use in independent scientific research to researchers upon reasonable request (lukas.mayer@i-med.ac.at). Data will be provided following review and approval of a research proposal (including a statistical analysis plan) and completion of a data sharing agreement.

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