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Long-Term Impairment From Irritant-Induced Occupational Asthma

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Objective: The aim of the study is to assess the long-term physical condition, health-related quality of life, employment, and work ability of irritant-induced asthma (IIA) patients. **Methods:** Forty-three IIA patients completed a follow-up questionnaire a median of eight (interquartile range 4–11) years after asthma diagnosis. We compared their results with those of 43 low-molecular-weight (LMW) sensitizer-induced occupational asthma (OA) patients and those of 206 adult-onset asthmatics in the general population. **Results:** Of the IIA patients, 40% reported depressive symptoms. Of the <65-year-olds, 56% were employed, of whom 39% assessed their work ability as limited. IIA patients had more difficulty climbing several flights of stairs than LMW-induced OA patients (70% vs 47%, OR = 4.83 95% CI: 1.51–15.47). Most of the IIA patients' outcomes were inferior to those of the adult-onset asthmatics in the general population. **Conclusions:** IIA prognosis appeared poor but resembled that of LMW-induced OA.

Keywords: health-related quality of life, IIA, irritant-induced asthma, irritants, occupational asthma, prognosis

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In remembrance of our colleague Jouko Remes.

The data that support the findings of this study are not openly available due to reasons of sensitivity and are archived in the repository of Finnish Institute of Occupational Health.

The authors adhered to the STROBE Guidelines.

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LEARNING OUTCOMES

- Better understanding of the need for close monitoring and active support after irritant exposures
- Awareness of the wide-ranging impairment associated with irritant-induced occupational asthma
- Identification of patients who require mental health support or physical rehabilitation

Workplace sensitizers can cause occupational asthma (OA) via immunologic mechanisms, whereas respiratory irritants are considered to generate irritant-induced asthma (IIA) via irritant mechanisms.[1–3] The European Academy of Allergy and Clinical Immunology (EAACI) position paper recognized acute, subacute, and low-dose IIA phenotypes.[2] The EAACI paper claimed that there can be sufficient evidence of a causal relationship between occupational exposures and the development of asthma in individual cases for the first two of these phenotypes.[2] The most recent surveillance data have suggested that acute IIA accounts for 4–15% of new-onset OA cases.[4–6]

OA is associated with a poor prognosis,[7–11] but IIA has remained poorly known: Only one study has evaluated the long-term outcome of acute IIA.[12] Previously, we observed that IIA patients displayed poorer asthma control than those with sensitizer-induced OA shortly after OA diagnosis.[13] In another study, we observed that poor asthma symptom control tends to be a long-lasting status among IIA patients.[14]

In the current study, we aimed to evaluate whether these poor results concern IIA patients' long-term physical capacity, health-related quality of life (HRQoL), employment, and work ability. Our secondary aim was to assess whether the prognosis of IIA differs from that of low-molecular-weight (LMW) sensitizer-induced OA. Finally, we aimed to compare IIA patients' outcomes to those of adult-onset asthmatics in the general population.

METHODS

Study Design

We carried out a systematic search to identify patients who were diagnosed with IIA in 2004–2018 at a tertiary outpatient clinic, the Finnish Institute of Occupational Health (FIOH).[13,15] These patients had been evaluated at FIOH (*baseline*), and a multidisciplinary panel of pulmonologists, occupational health physicians, and occupational toxicologists had given an initial IIA diagnosis. Our group, consisting of an occupational toxicologist, an occupational health physician (KK), and two pulmonologists (JL, IL) confirmed these diagnoses.

The *diagnostic criteria* were 1) no evidence of active asthma in adulthood before the exposure; 2) exposure to a high concentration of an airborne irritant; 3) occurrence of asthma symptoms in a close temporal relationship with the exposure; 4) asthma verification by reversible obstruction or nonspecific bronchial hyperresponsiveness; 5) persistence of symptoms for ≥3 months; and 6) no other pulmonary

disorder that explained the symptoms. These criteria are in accordance with those of the EAACI position paper.[2]

Sixty-nine patients met our criteria for IIA, of whom 30 had only one high-level exposure event within 24 hours and 39 had repeated exposure events to high levels of irritants during a period of more than 24 hours.[13,15] We classified the first group as acute IIA and the latter group as subacute IIA. In the case of most of the identified patients, asthma diagnosis had been confirmed and inhaled corticosteroids initiated before their referral to FIOH.[13]

Our reference group comprised 89 patients who had been diagnosed with LMW-induced OA at FIOH in 2006–2018. Their diagnosis had been verified by a specific inhalation challenge. In our previous study, their demographic characteristics and work history had resembled those of IIA patients.[13]

We notified the previously identified IIA and LMW-induced OA patients of the follow-up study.[13] Forty-three of those with IIA (62%) and 43 of those with LMW-induced OA (48%) were willing to participate and consented to filling out a follow-up questionnaire. A research nurse interviewed these participants between June and October 2020 by telephone. We also gave the respondents the option of completing the questionnaire online or posting it to us.

The Finnish Institute of Health and Welfare (THL) carried out the Health 2011 Survey to collect data on the health, functional capacity, and welfare of the Finnish general population.[16] This survey had 6740 respondents, yielding a response rate of 67%.[16] Two hundred six participants reported having been diagnosed with asthma by a physician between the ages of 21 and 64, which corresponded to the age range of our respondents. The THL Biobank granted us access to its data on these participants (ID: THLBB2021_47). They represented the population-level adult-onset asthma in this study, to which we compared the results of the OA patients. Figure 1 depicts our study design. The study followed the STROBE Guidelines for observational studies (Supplemental Digital content STROBE Statement, http://links.lww.com/JOM/B578).

Data and Definitions

Smoking history was divided into nonsmokers, current smokers, and ex-smokers. Current and ex-smokers had smoked ≥10 pack years, and ex-smokers had quit ≥6 months previously. *Unhealthy alcohol consumption* was evaluated using the AUDIT-C screen test.[17]

Physical condition was screened by the participant's self-assessment of their ability to climb stairs and walk 2 km without resting.[16,18] The Finnish modification of the 13-item Beck Depression Inventory (BDI-13) screens *depressive symptoms*, and its score ranges from 0 to 39; 0 to 4 represents no depressive symptoms, 5 to 7 mild symptoms, 8 to 15 moderate symptoms, and 16 to 39 severe symptoms.[16,19]

HRQoL was assessed using the 15D instrument, which is a generic, multidimensional, standardized, self-administered measure that assesses 15 aspects of HRQoL (mobility, vision, hearing, breathing, sleeping, eating, speech, excretion, usual activities, mental function, discomfort and symptoms, depression, distress, vitality, and sexual activity).[20] This instrument measures a single index score that represents overall HRQoL, and the scores range from 0 to 1 (0 = no longer alive, 1 = full health). It is estimated that the minimum clinically important difference in the total 15D score is +/− 0.015 in cross-sectional comparisons.[21] The 15D instrument also contains within-dimension level values, which can be viewed as the respondent's profile.

The respondent's *work status* was divided into the following four categories: 1) employed, 2) unemployed, 3) retired, and 4) other (including sick leave, studying, homemaker and military service). We obtained an access to the Finnish Centre for Pensions' Earnings Register's and found the employment of the 36 respondents with IIA and 42 respondents with LMW-induced OA who gave their written, informed consent for this analysis. According to the Finnish Centre for Pensions, this register "contains information on the individual's work career that gives entitlement to an earnings-related pension."[22] We present the cumulative proportion of time for which the individual was employed after OA diagnosis until they either completed this questionnaire, began receiving an old-age pension, or turned 65, which is the common age for old-age pension in Finland.[23]

Those who were currently employed assessed their Work Ability Score and predicted their own future work ability.[24] For the *Work Ability Score*, the respondents compared their current work ability to their lifetime best, using scores ranging from 0 to 10; 0 to 5 represented poor, 6 to 7 moderate, 8 to 9 good, and 10 excellent work ability.[24] For *future work ability*, the respondents evaluated whether they believed they would be fit for their current work in 2 years' time.

The IIA patients also completed *the Asthma Control Test (ACT),*[25] which screens asthma symptom control. Scores range from 5 to 20, and a score of ≤19 represents poor symptom control.[25,26] Our previous publication reports these findings in more detail[14]; in this study, we only included them in the analysis of the results of the respondents with IIA.

Statistical Analysis

We applied IBM SPSS Statistics for Macintosh, Version 28.0 (IBM Corp., Released 2021, Armonk, NY) in the statistical analyses. We expressed categorical values as counts and percentages and applied

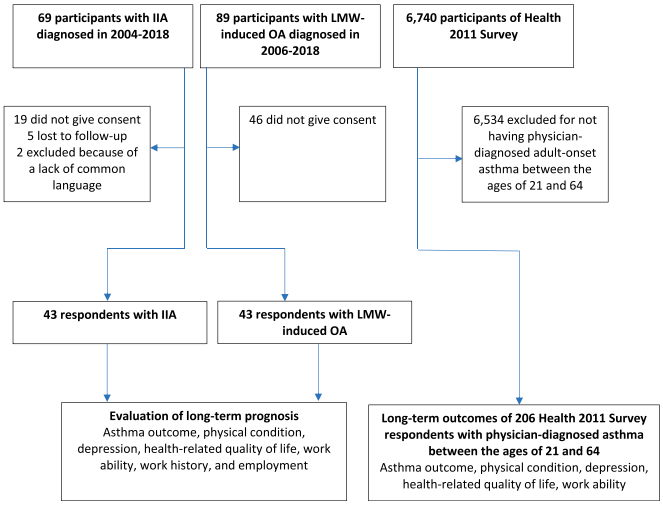

FIGURE 1. Study design and patient selection.

TABLE 1. Causative Agents of the Respondents With Irritant-Induced Asthma and Low-Molecular-Weight Sensitizer-Induced Occupational Asthma

Irritant	*N* = 43	Low-Molecular-Weight Agent	*N* = 43
Acid aerosols or fumes	9	Isocyanates	19
Mixtures	8	Acrylates	5
Dusts	7	Metal Working fluids	4
Base aerosols or fumes	5	Colophony	3
Endotoxins	4	Anhydrides	2
Other irritant chemicals	4	Aldehydes	2
Inorganic gases	3	Epoxy	1
Mixtures of acid and base aerosols or fumes	2	Other low-molecular-weight agents	7
Oxidizing agents	1		

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Fisher's exact test. If the quantitative data followed a normal distribution, we presented the results as means and standard deviations (SD). If these assumptions were contradicted, we showed them as medians and interquartile ranges (IQRs). In the former case, we used the independent samples *t* test and, in the latter, the Mann-Whitney *U* test.

We performed logistic regression analyses on the nominal variables and analysis of covariance on the 15D. The models were adjusted for sex, time since asthma diagnosis, age, body mass index (BMI), smoking history and level of asthma treatment (no medication, only inhaled corticosteroids [ICS], ICS plus add-on therapy) at the time of the questionnaire. The last factor estimated the asthma severity. The Spearman correlation r_s between the continuous variables was also calculated. *P* values of <0.05 and a 95% confidence interval (CI) with a lower limit of >1 or upper limit of <1 was regarded as significant.

Ethics

The ethics committee of the Department of Medicine, Helsinki University Central Hospital, Finland (approval number HUS/611/2020) approved this study. We obtained written informed consent for publication from each participant. No medical interventions were performed at FIOH.

RESULTS

Characteristics of OA Patients at Baseline

Table 1 displays the causative agents of the respondents with OA. The respondents and the nonrespondents were comparable in both OA groups, except for a shorter interval between baseline and follow-up ($P = 0.024$) and a lower ratio of forced expiratory volume in first second and forced vital capacity (FEV1/FVC) ($P = 0.042$) among the respondents with IIA (Supplemental Digital Content Table 1, http://links.lww.com/JOM/B579). The comparison of the baseline characteristics of the respondents with IIA and LMW-induced OA revealed that the former had a shorter duration of asthma symptoms ($P = 0.002$), a lower FEV1/FVC ratio ($P = 0.042$), more frequent use of daily short-acting beta agonists ($P = 0.002$), and more frequent exacerbations ($P = 0.014$) (Supplemental Digital Content Table 1, http://links.lww.com/JOM/B579). Otherwise, these groups appeared comparable (Supplemental Digital Content Table 1, http://links.lww.com/JOM/B579).

Long-Term Physical Capacity, Depressive Symptoms, and HRQoL

Table 2 presents the respondents' demographic characteristics and asthma outcome at follow-up. Among the respondents with IIA, the average time since asthma diagnosis was 7.8 (SD 4.4) years. Eighteen (42%) of these had acute IIA and 25 (58%) had subacute IIA. Two (5%) were ≥65 years old, 11 (26%) had a BMI of ≥30 kg/m^2, and 19 (44%) had a smoking history of ≥10 pack years. Thirty-six (86%) used ICS, 30 (70%) had an add-on therapy, and 38 (88%) reported asthma symptoms during the last year. Thirty (70%) had difficulties climbing several flights of stairs, 18 (42%) had difficulties walking 2 km, and 17 (40%) reported depressive symptoms (Table 3).

Those with IIA had a shorter time since asthma diagnosis than others, and the group contained less ≥65-year-olds (5% vs 26%) than the LMW-induced OA group. Otherwise, the demographic and prognostic outcomes of those with IIA resembled those of the respondents with LMW-induced OA (Table 2 and Table 3, respectively). Compared to the population-level adult-onset asthmatics, the respondents with IIA were more frequently male, used more intensive medication, and more often had asthma symptoms (Table 2). Regarding prognostic outcomes, those with IIA more frequently had a poor physical capacity than the others (Table 3). However, after adjustments, only difficulty

TABLE 2. Demographic Characteristics and Asthma Outcome of Participants With Irritant-Induced Asthma, Low-Molecular-Weight Sensitizer-Induced Occupational Asthma, and Population-Level Adult-Onset Asthma

Characteristic	IIA *N* = 43	LMW-Induced OA *N* = 43	IIA vs LMW-Induced OA *P* Value	Population-Level Adult-Onset Asthma *N* = 206	IIA vs- Population-Level Adult-Onset Asthma *P* Value
Time since asthma diagnosis, years			0.002		<0.001
Mean (SD)	7.8 (4.4)	11.3 (5.8)		12.0 (9.2)	
Demographic characteristics					
Age			0.805		0.803
Mean (SD)	53.5 (9.4)	54.1 (12.9)		52.7 (9.4)	
Male	37 (86%)	29 (67%)	0.072	68 (33%)	<0.001
BMI, kg/m^2			0.480		0.065
Median (IQR)	28.1 (26.0–30.2)	28.1 (24.3–31.7)		27.6 (23.7–30.8)	
Smoking history of ≥10 pack years	19 (44%)	27 (63%)	0.130	69 (33%)	0.220
Asthma outcome					
Asthma medication			1.000		<0.001
• No medication	7 (16%)	7 (16%)		90 (44%)	
• ICS	6 (14%)	6 (14%)		49 (24%)	
• ICS + add-on	30 (70%)	30 (70%)		67 (33%)	
Asthma symptoms over 1 year	38 (88%)	33 (77%)	0.255	118 (57%)	<0.001

BMI, body mass index; ICS, inhaled corticosteroids; IIA, irritant-induced asthma; IQR, interquartile range; LMW, low-molecular-weight sensitizer; SD, standard deviation.

TABLE 3. Long-Term Prognostic Outcomes of Participants With Irritant-Induced Asthma, Low-Molecular-Weight Sensitizer-Induced Occupational Asthma, and Population-Level Adult-Onset Asthma

Characteristic	IIA *N* = 43	LMW-Induced OA *N* = 43	IIA vs LMW-Induced OA *P* Value	Population-Level Adult-Onset Asthma *N* = 206	IIA vs- Population-Level Adult-Onset Asthma *P* Value
Physical condition					
Difficulties climbing several flights of stairs	30 (70%)	20 (47%)	0.048	44 (21%)	<0.001
Difficulties walking 2 km	18 (42%)	18 (42%)	1.000	34 (17%)	<0.001
Mental health					
Depressive symptoms[a]	17 (40%)	15 (35%)	0.824	51 (25%)	0.090
Health-related quality of life					
15D score[b]			0.166		0.002
Mean (SD)	0.841 (0.119)	0.874 (0.087)		0.902 (0.088)	

[a]Depressive symptoms screened using the Finnish modification of the 13-item Beck depression Inventory.[19]
[b]15D score represents a health-related quality of life index score from 0 to 1 (0 = dead, 1 = full health).[20]
IIA, irritant-induced asthma; LMW, low-molecular weight sensitizer; OA, occupational asthma; SD, standard deviation.

climbing stairs differed significantly between the IIA and LMW-induced OA patients (70% vs 47%, odds ratio [OR] 4.83, 95% CI: 1.51–15.47) and between the IIA and population-level adult-onset asthmatics (70% vs 21%, OR = 12.83, 95% CI: 4.77–34.50) (Supplemental Digital Content Table 2.1, http://links.lww.com/JOM/B579). Depressive symptoms were common among all the participants.

Figure 2 illustrates the 15D profiles of each study group. The respondents with IIA and those with LMW-induced OA showed no statistically significant differences in terms of total score or any of the 15 dimensions. In contrast, the respondents with IIA had a lower total score than the population-level adult-onset asthmatics and a lower score in and 8 of the 15 dimensions (mobility, hearing, breathing, sleeping, speech, usual activities, vitality, and sexual activities). The adjusted 15D score did not change the result (adjusted mean difference of −0.043, $P = 0.021$ (Supplemental Digital Content Table 2.2, http://links.lww.com/JOM/B579). Social characteristics were also similar across the groups (Supplemental Digital Content Table 3, http://links.lww.com/JOM/B579).

Employment and Work Ability

Twenty-three (53%) of the respondents with IIA (53%), 18 (42%) of those with LMW-induced OA, and 131 (64%) of those with population-level adult-onset asthma were employed at follow-up (Table 4). Among the <65-year-olds, the respective figures were 56%, 56%, and 64%, respectively. The median surveillance time in the data of the Finnish Centre for Pensions' Earnings Register was 5.7 (IQR 3.1–10.0) years in IIA and 5.9 (IQR 5.8–11.3) years in LMW-induced OA. Thirty-one percent of those IIA patients had been employed throughout the study period, and 53% had been employed for ≥67% of this time. The cumulative employment of the IIA patients was comparable to that of the LMW-induced OA patients (Table 4).

An equal number of respondents with IIA and respondents with LMW-induced OA had changed their work tasks, workplaces, and occupations since their asthma diagnosis. Six respondents with IIA and two with LMW-induced OA were currently employed and had no job modifications. We could not rule out current exposure to a causal agent for three of those with IIA and two of those with LMW-induced OA. Twenty-one (49%) IIA patients and 22 (51%) LMW-induced OA patients had had vocational rehabilitation, such as retraining or work trial, after the diagnosis. In both OA groups, half of the respondents reported self-assessed loss of income after the onset of asthma.

Sixty-one percent of the respondents with IIA who were employed believed they would be fit for current work in 2 years' time, and 39% of them assessed their current Work Ability Score to be ≤7 (ie, poor or moderate work ability). The corresponding figures were 75% and 19% for the LMW-induced OA patients and 88% and 19% for the population-level adult-onset asthmatics. In both OA groups,

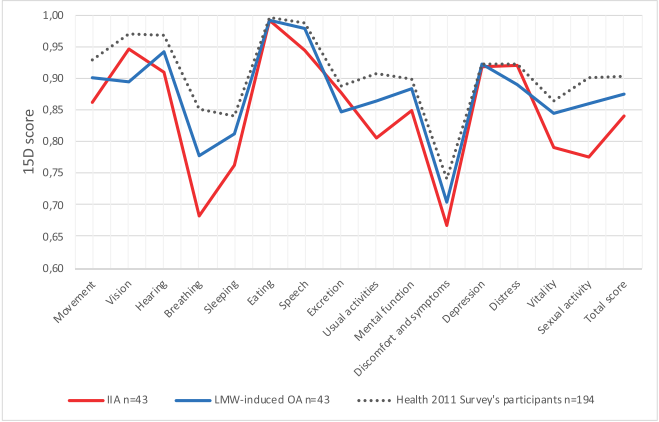

FIGURE 2. Health-related quality of life (15D) profiles of irritant-induced occupational asthma, low-molecular-weight agent-induced occupational asthma and population-level adult-onset asthma. 15D profile contains 15 dimensions of health-related quality of life.[20] Average within-dimension levels of each group.

TABLE 4. Employment and Self-assessed Work Ability of Participants With Irritant-Induced Asthma, Low-Molecular-Weight Sensitizer-Induced Occupational Asthma, and Population-Level Adult-Onset Asthma

Characteristic	IIA $N = 43$[a]	LMW-Induced OA $N = 43$[a]	IIA vs LMW-Induced OA *P* Value	Population-Level Adult-Onset Asthma $N = 206$[a]	IIA vs Population-Level Adult-Onset Asthma *P* Value
Employment					
Current work status			0.629		0.129
• Employed	23 (53%)	18 (42%)		131 (64%)	
• Unemployed	3 (7%)	4 (9%)		14 (7%)	
• Retired	11 (26%)	16 (37%)		52 (25%)	
• Other	6 (14%)	5 (12%)		9 (4%)	
After onset of asthma					
• Same job	18 (42%)	15 (35%)	0.658	NA	NA
• Changed work task	12 (28%)	12 (28%)	1.000	NA	NA
• Changed workplace	18 (42%)	17 (40%)	1.000	NA	NA
• Changed occupation	15 (35%)	17 (40%)	0.824	NA	NA
Loss of income after onset of asthma	22 (51%)	19/41 (46%)	0.670	NA	NA
Proportion of time employed after OA diagnosis[b]			0.448	NA	NA
• 100%	11/34 (31%)	7/42 (17%)			
• 67–99%	8/34 (22%)	10/42 (24%)			
• 34–66%	7/34 (19%)	7/42 (17%)			
• ≤33%	10/34 (28%)	17/42 (41%)			
Self-assessed work ability[c]					
Fit for current work in two years' time	14 (61%)	12 (75%)	0.495	115 (88%)	0.003
Work ability score	$n = 23$	$n = 16$	0.114	$n = 131$	<0.001
Mean (SD)	7.0 (2.0)	8.2 (0.8)		8.4 (1.6)	
Work-exacerbated symptoms			0.914		
• No symptoms	4 (17%)	4 (25%)		NA	NA
• Similar at work and when off work	6 (26%)	2 (13%)		NA	NA
• Worse at work	13 (57%)	10 (63%)		NA	NA

[a]Unless otherwise specified, 43 IIA patients, 43 LMW-induced OA patients, and 206 participants with population-level adult-onset asthma patients answered the questionnaire.
[b]Data of the Earnings Register of the Finnish Centre for Pensions. Two of the 36 participants with IIA had retired immediately after their diagnosis and were excluded from the analysis.
[c]Of those employed, 23 IIA patients, 16 LMW-induced OA patients and 131 participants with population-level adult-onset asthma assessed their work ability.
IIA, irritant-induced asthma; IQR, interquartile range; LMW, low-molecular-weight sensitizer; NA, not available; OA, occupational asthma; SD, standard deviation.

three-fifths of those employed reported work-exacerbated asthma symptoms in their current work.

Factors Contributing to Poor Long-Term Outcomes of Irritant-Induced Asthma

The ACT score correlated positively with both the 15D score and the Work Ability Score ($r_s = 0.498$, $P < 0.001$ and $r_s = 0.483$, $P = 0.020$, respectively). The BDI-13 score correlated negatively with these outcomes ($r_s = -0.780$, $P < 0.001$ and $r_s = -0.460$, $P = 0.027$, respectively). In the same way, the 24 respondents with IIA and an ACT score of ≤19 had a poorer 15D score than those 19 with an ACT score of ≥20 (mean of 0.794 [SD 0.135] vs 0.899 [SD 0.058], $P = 0.002$), while those with depression had a lower 15D score than the others (mean of 0.751 [SD 0.121] vs 0.899 [SD 0.073], $P < 0.001$). Employment, time since asthma diagnosis, age, BMI, and number of pack years showed only a negligible correlation or no correlation with either one. Prognostic outcomes, such as depression, physical condition, health-related quality of life, or employment after the diagnosis, did not differ between those with short period (≤7.8 years) and those with long period (>7.8 years) of follow-up.

Although the respondents with the poorest long-term outcomes tended to be those with acute IIA, difficulties walking 2 km (67% vs 24%, $P = 0.011$) and changes in work tasks (50% vs 12%, $P = 0.014$) were the only factors to differ significantly between those with acute and subacute IIA (Supplemental Digital Content Table 4, http://links.lww.com/JOM/B579).

DISCUSSION

We evaluated the prognosis of 43 IIA patients and found poor long-term outcomes among them. A median of 8 years after their asthma diagnosis, many of these patients assessed their own physical condition as limited, and 40% reported depressive symptoms. The IIA patients had impaired HRQoL, which concerned multiple aspects of life. Their cumulative employment had remained fairly good since their IIA diagnosis. However, 39% of those currently employed had diminished self-assessed work ability. Poor asthma symptom control and depressive symptoms were associated with impaired HRQoL and work ability. Despite minor differences, the long-term IIA outcomes resembled those of LMW-induced OA. In contrast, the IIA patients tended to show inferior outcomes to those of the self-reported population-level adult-onset asthmatics.

Our previous article found that uncontrolled asthma was common among IIA patients.[14] Otherwise, only a limited number of studies have analyzed the long-term outcomes of IIA. Malo et al[12] examined 35 individuals with an acute IIA mean of 13.6 years after exposure and found that they had high symptom scores and decreased quality of life and that one-third of them had psychiatric comorbidities. Rescue and recovery workers of the World Trade Center (WTC) catastrophe had a high incidence of asthma after exposure to irritant agents.[27] The WTC workers still have poor asthma control, poor asthma-related quality of life, and frequent mental health disorders several years after exposure.[27–30] The results of our current study support these previous findings.

In general, patients whose asthma is exacerbated or caused by the workplace environment (ie, work-related) tend to show poorer outcomes and a greater use of healthcare than those with nonwork-related asthma.[11,31–33] In the same way, our study suggests that the long-term outcomes of IIA are poorer than those of adult-onset asthmatics in the general population. We are aware that there were differences among our selected study populations, because the diagnosis of the OA patients was verified in the specialist center, whereas the diagnosis of the Health 2011 Survey participants was based on self-reported

physician-diagnosed asthma. However, we aimed to demonstrate with this comparison, which is the burden of IIA is heavier than that of adult-onset asthma in the general population. Furthermore, our findings remained unchanged even when we adjusted for the level of asthma treatment (ie, asthma severity) (Supplemental Digital Content Tables 2.1 and 2.2, http://links.lww.com/JOM/B579).

Prior studies have shown that HRQoL tends to be reduced among those with work-related asthma.[7,9,10,34,35] In this study, we observed that although the respondents with IIA had a lower 15D score than those with LMW-induced OA, the difference was statistically insignificant. In contrast, the 15D instrument showed that the respondents with IIA had poorer HRQoL than the Health 2011 Survey's participants with adult-onset asthma. In follow-up studies, a difference of < -0.035 signifies a change toward "much worse."[21] This limit was clearly exceeded in the comparison of IIA patients and population-level adult-onset asthmatics. Lower HRQoL appeared comprehensive, as the poor results concerned several 15D dimensions.

Regarding employment, the previous literature has shown that OA and workplace interventions contribute to employment.[36] Finnish legislation requires employers to insure their employees against occupational diseases, and workers are entitled to compensation and, frequently, retraining, which might have a beneficial influence on employment. We observed that 56% of the <65-year-olds reported being currently employed in both OA groups and that of these, 26% of those with IIA and 11% of those with LMW-induced OA had no job modifications.

Only a few previous studies have had an equally long follow-up time to ours. Malo et al[12] noticed that 12 (34%) of their IIA patients were employed for a mean of 13.6 years after an inhalation accident. Other studies have included mostly diisocyanate-induced OA patients, and their employment has ranged from 44% to 91%, and 14% to 48% of those employed had remained in the same workplace 10 to 12 years after their OA diagnosis.[8,37–39]

The Finnish Centre for Pensions granted us access to its register data on employment for this study. We noticed that a third of the respondents with IIA had been employed throughout the period studied and more than a half had worked over two-thirds of the time. The cumulative employment of the IIA patients was comparable to that of the LMW-induced OA patients. Our questionnaire also revealed that IIA and LMW-induced OA patients were similar in terms of work history, vocational rehabilitation, and loss of income. Thus, according to our results, the socioeconomic outcome of IIA and LMW-induced OA patients was comparable.

On the other hand, we observed that the respondents with IIA had reduced work ability. Of those with IIA who were employed, two-fifths assessed their work ability as moderate or poor, and only three-fifths predicted that they would be fit for their current work in 2 years' time. A previous 3-year, register-based follow-up study by Kinnunen et al[24] detected that this level of self-assessed work ability predicted disability pension and long-term sickness absence among Finnish employees. However, our sample size was small, and as we did not include the nature of the work or comorbid conditions in our assessment of work ability, these findings should be interpreted with caution.

We observed that poor asthma symptom control and depressive symptoms were associated with impaired HRQoL and work ability, which is in accordance with the previous literature. Miedinger et al[10] found that respiratory symptoms and psychological distress correlated negatively with asthma-related quality of life among their participants with OA. Studies of the WTC workers[29,30] have also observed a connection between poor HRQoL and depressive symptoms. Piirilä et al,[8] in turn, noticed that those employed and those satisfied with life had fewer asthma symptoms and used less asthma medication than their counterparts among diisocyanate-induced OA patients. Several studies of adult-onset asthma also support our findings.[33,40–43] Some additional factors might remain unidentified, as Knoeller et al[35] showed that individuals with work-related asthma had poorer HRQoL at all levels of asthma control.

Finally, this study included both acute and subacute IIA cases. Previously, we observed that the short-term outcomes of these subtypes strongly resemble each other.[13] This study found that the long-term prognosis of acute and subacute IIA patients also tends to be similar. We are not aware of any other publications that have addressed the prognosis of subacute IIA.

Strength and Limitations

There is very little literature on IIA. To our knowledge, ours is the largest follow-up study of IIA patients to date. We were able to compare the long-term outcomes of IIA to those of LMW-induced OA patients. In addition, we had objective data on the employment of the OA patients.

However, our study had several limitations. First, the current characteristics were based on the results of a questionnaire rather than objective data, apart from the data regarding employment. Second, the comparison of the OA cases and the Health 2011 Survey participants might have been affected by selection bias toward more severe asthma among the former because the OA patients were evaluated in a tertiary center by pulmonologists whereas the latter self-reported their physician-diagnosed asthma. Those with more severe outcomes might also more actively participate in follow-up studies. However, the results did not change when we separately analyzed the participants using ICS or ICS plus adds-on treatment. In addition, the only significant differences between the respondents and the nonrespondents were a shorter time since FIOH's evaluation and a lower FEV1/FVC ratio among the respondents with IIA.

Third, the background characteristics of the groups differed in some respects: Time since asthma diagnosis was shorter and the FEV1/FVC ratio lower among those with IIA. Those with IIA also tended to more frequently be male and less frequently have a smoking history of ≥10 pack years than those with LMW-induced OA. Fourth, a deeper analysis of comorbid diseases and psychiatric disorders might have been beneficial. Fifth, we only had the current score of the applied instruments (ie, Work Ability Score and 15D score), and thus were unable to analyze the cause-response relationship between OA diagnosis and the long-term outcome.

CONCLUSIONS

This study showed that poor asthma outcome and impaired physical capacity and HRQoL are common findings among IIA patients several years after their asthma diagnosis. Their employment appears to remain fairly good, despite possible limitations to the IIA patients' self-assessed work ability. According to our study, the long-term prognosis of IIA is comparable to that of LMW-induced OA. Our findings imply that IIA patients are likely to benefit from close monitoring and active support in order to avoid poor outcomes. Better asthma symptom control, good care of mental health comorbidities, and physical rehabilitation are potential targets for clinicians as these factors appear to contribute to prognosis.

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