ORIGINAL ARTICLE

Artificial stone-associated silicosis in China: A prospective comparison with natural stone-associated silicosis

NA WU, CHANGJIANG XUE, SHIWEN YU AND QIAO YE

Department of Occupational Medicine and Toxicology, Clinical Center for Interstitial Lung Diseases, Beijing Chao-Yang Hospital, Capital Medical University, Beijing, China

ABSTRACT

Background and objective: We recently noted a dramatic increase in the number of patients with accelerated silicosis associated with exposure to artificial stone dust. Therefore, the natural history of artificial stone-associated silicosis was compared with that of natural stone-associated silicosis.

Methods: A total of 18 patients with artificial stone-associated silicosis and 63 with natural stone-associated silicosis were diagnosed sequentially in 2018 and followed up for a period of 6–12 months. Data were collected from clinical charts.

Results: The median duration of exposure prior to onset of symptoms of silicosis was shorter for patients who had been exposed to artificial stone dust (6.4 vs 29.3 years, \( P < 0.01 \)). Four of the 18 patients experienced rapid deterioration in lung function over the follow-up period, with declines in pre-bronchodilator FVC of 587 (210–960) mL/year and FEV\(_1\) of 625 (360–860) mL/year. GGO, PMF, emphysema and pulmonary artery widening were more frequently observed on computed tomography scans of patients with artificial stone-associated silicosis than of those with natural stone-associated silicosis. Approximately 38.9% of the patients with artificial stone-associated silicosis were lung transplant candidates and 27.8% died, both rates being significantly higher than in patients with natural stone-associated silicosis (3.2% and 0%, both \( P < 0.01 \)).

Conclusion: Compared to natural stone-associated silicosis, artificial stone-associated silicosis was characterized by short latency, rapid radiological progression, accelerated decline in lung function and high mortality.

Key words: artificial stone, progressive massive fibrosis, pulmonary function, respirable crystalline silica, silicosis.

SUMMARY AT A GLANCE

High silica content of artificial stone and uncontrolled dry cutting and grinding presents as a high risk of developing accelerated silicosis. Compared to natural stone-associated silicosis, artificial stone-associated silicosis was characterized by short latency, rapid radiological progression, accelerated decline in lung function and high mortality in this study.

INTRODUCTION

Silicosis is a progressive, fibrotic, occupational lung disease, which results from inhalation of respirable crystalline silica (RCS).\(^1\)\(^2\) Occupations traditionally associated with increased risk of silicosis include glass and pottery making, mining and quarrying, sandblasting and construction trades that generate silica dust through stone or concrete work.\(^3\) Silicosis in workers exposed to artificial quartz conglomerates containing high proportions of crystalline silica particles has been a topic of investigation in recent years.\(^4\)\(^–\)\(^9\)

Artificial stone, also termed engineered, agglomerated or reconstituted stone or quartz conglomerate, is a relatively new, increasingly popular building material that is used primarily to fabricate kitchen and bathroom countertops.\(^10\)\(^–\)\(^11\) Artificial stone is a composite of quartz, the major filler, and coloured glass, shells, metals or mirrors bound together by a polymer resin.\(^12\)

Artificial stone became commercially available in 1986, and the first report of artificial stone-associated silicosis caused by stonemasonry was published in Italy in 2010.\(^11\) Since then, increasing numbers of cases have been reported from Spain, Israel, Australia, Turkey and the USA.\(^4\)\(^–\)\(^9\) Artificial stone has been available in China since the early 2000s, but no reports of artificial stone-associated silicosis in China have been published. We recently noted a marked increase in the number of patients with artificial stone-associated silicosis.

At 70–90%, the silica content of artificial stone is far higher than that of natural stone (approximately 3% in...
marble and 30% in granite). Thus, the risk of exposure to artificial quartz conglomerates appears to be higher than that of exposure to natural stone dust, and the associated silicosis may differ significantly in its latency and clinical characteristics. To determine whether artificial stone-associated silicosis differs from natural stone-associated silicosis, we studied a series of patients with newly diagnosed silicosis who attended our hospital, including 18 who were exposed to artificial stone dust and 63 who were exposed to natural stone dust.

METHODS

Study cohort
From January to December 2018, 81 patients with newly diagnosed silicosis were sequentially recruited from the Department of Occupational Medicine and Toxicology, Beijing Chao-Yang Hospital. All patients completed a standardized questionnaire to collect information on their occupational histories (Table S1 in Supplementary Information). No workplace exposure monitoring data were available. All patients were diagnosed according to the criteria for pneumoconiosis of the 2011 International Labour Organization classification and the International Classification of HRCT for Occupational Environmental Respiratory Diseases (ICOERD). The patients were divided into two groups: 18 with artificial stone-associated silicosis and 63 with natural stone-associated silicosis.

This work was conducted at Beijing Chao-Yang Hospital with approval from the human research ethics committee of Beijing Chao-Yang Hospital, Capital Medical University. Informed consent was documented in writing.

Pulmonary function tests
The pulmonary function examination was standardized according to the American Thoracic Society (ATS)/European Respiratory Society (ERS) recommendations and included spirometry, body plethysmography and the measurement of carbon monoxide transfer factor of the lungs utilizing the single-breath method.

High-resolution computed tomography
High-resolution computed tomography (HRCT) scans in patients were performed with 0.625-mm sections, a 1-s scan time and a 10-mm interval in the apex base scans with inclusion of both lungs in the field of view.

Statistical analysis
The mean values for relevant patient characteristics and pulmonary function variables are expressed as mean ± SD. The Mann-Whitney U-test was used to assess differences between the two groups, as appropriate. The distribution of radiological opacities was evaluated using the chi-square test. A P-value of < 0.05 denotes statistical significance. All data were analysed with SPSS version 21.0 (IBM SPSS, Armonk, NY, USA).

RESULTS

Characteristics of the study population
Table 1 displays the relevant clinical and other characteristics of patients, stratified by type of silicosis. Patients with artificial stone-associated silicosis were younger than patients with natural stone-associated silicosis and had shorter exposure durations. The decision to place a patient on the waiting list for lung transplantation was made in accordance with a consensus document for selection of lung transplant candidates and a previous study. However, candidates in both groups failed to undergo lung transplantation within the study period for lack of medical insurance. During a follow-up period of 6–12 months, five patients (27.8%) with artificial stone-associated silicosis died. A higher incidence of spontaneous pneumothorax, lung transplant candidates and mortality was found in patients with artificial stone-associated silicosis than in those with natural stone-associated silicosis (all P < 0.05).

Occupational dust exposure
The 63 patients with natural stone-associated silicosis were all local residents. Twenty-nine patients had been exposed to silica dust in the processing of jade and 34 patients engaged in mining and quarrying. The jade-processing factories were functional from the 1970s to the 1990s, and the mining plants had been open from the 1970s to the 2000s. These enterprises used lower level production technologies and occupational protection strategies. Eighteen patients (28.6%) with natural stone-associated silicosis reported using disposable masks during all working hours, 27 (42.8%) reported using disposable masks 3–5 h per day during working hours and 18 (28.6%) working without any personal respiratory protection.

Of the 18 patients with artificial stone-associated silicosis, 5 were from Fujian province, 4 from Guangdong province, 4 from Anhui province, 2 from Shanghai, 2 from Jiangsu province and 1 from Zhejiang province. Four patients (22.2%) from the same artificial stone factory reported using disposable masks during cutting, polishing and grinding activities and applying water curtains. Fourteen patients (77.8%) performed cutting and home installation of kitchen and bathroom countertops without any respiratory protection.

HRCT findings
The patients were classified into groups with complicated or simple silicosis on the basis of disease extent, as determined by HRCT. Complicated silicosis, or accelerated silicosis with progressive massive fibrosis (PMF), was defined as the presence of a large opacity or coalescence larger than 1.5 cm in diameter. On that basis, 14 patients (77.8%) exposed to artificial stone were diagnosed as having complicated silicosis (Table 1). The incidence of ground-glass opacities (GGO), large opacities, emphysema and pulmonary artery widening was significantly higher in patients with artificial stone-associated silicosis than in those with natural stone-associated silicosis (all P < 0.05). In contrast, the incidence of rounded opacities and
medialstinal lymphadenopathy was significantly lower in patients with artificial stone-associated silicosis (all \( P < 0.05 \) (Table 2).

Well-defined rounded opacity and mediastinal lymphadenopathy were more frequently identified in patients with natural stone-associated silicosis, and during a follow-up period of 6–12 months, no change was found in the size, density or distribution of the opacities on HRCT in the 63 patients with natural stone-associated silicosis (Fig. 1A,B). Two patients with artificial stone-associated silicosis had extensive faint ground-glass nodules, similar to hypersensitivity pneumonia (Fig. 1C). Severe radiological abnormalities in 13 patients with artificial stone-associated silicosis were characterized by bilateral upper lobe fibrosis and volume loss with bilateral patchy consolidation, indistinct boundaries and ground-glass attenuation, consistent with PMF (Fig. 1D). In addition, during the follow-up of 6–12 months, HRCT showed rapid radiological progression in 13 patients (72.2%) with artificial stone-associated silicosis (Fig. 2).

**Changes in pulmonary function**

Pulmonary function was tested again in four patients with artificial stone-associated silicosis, and rapid deterioration in lung function was found over the follow-up period of 6–12 months, with a decline in pre-bronchodilator forced expiratory volume in 1 s (FEV\(_1\)) of 587 (210–960) mL/year and forced expiratory volume in 1 s (FEV\(_1\)) of 625 (360–860) mL/year (Table 3). Nine patients underwent pulmonary function tests at the time of the initial diagnosis but did not
Figure 1  Chest high-resolution computed tomography (HRCT) of four patients with differing findings. (A, B) Patients with natural stone-associated silicosis. (C, D) Patients with artificial stone-associated silicosis. (A) A 52-year-old man had been handling raw materials containing silica for 15 years. HRCT showed small, diffuse, well-defined nodules in both lungs. (B) A 59-year-old man had been mining for 20 years. HRCT showed large well-defined opacities with distinct borders surrounded by radiating lines. (C) A 22-year-old man had been cutting artificial stone 6 years. HRCT showed extensive centrilobular ground-glass nodules, similar to those seen in hypersensitivity pneumonia. (D) A 25-year-old man had been cutting and polishing bathroom and kitchen countertops for 5 years. HRCT showed bilateral patchy consolidation, indistinct boundaries and ground-glass attenuation, consistent with progressive massive fibrosis.

Figure 2  A 37-year-old man had been cutting, polishing and home installing artificial stone for 4 years. High-resolution computed tomography (HRCT) showed rapid radiological progression. (A) HRCT image showed patchy, irregular opacities of varying density. (B) HRCT showed a reduction in the volume of the lungs and features characteristic of progressive massive fibrosis 7 months later.
undergo them again 6 months later, when they experienced severe respiratory distress.

During the follow-up period, pulmonary function in 51 patients with natural stone-associated silicosis declined to a pre-bronchodilator FVC of 94.7 (−210 to 320) mL/year and FEV₁ of 84.3 (−80 to 300) mL/year (Tables 4, S2 in Supplementary Information).

**Particle analysis**

Four artificial stone dust samples collected from one of the factories were analysed using X-ray powder diffraction. All samples were found to have a high silica content of above 90%. The particles derived from the samples had a high proportion of small particles (diameter < 5 μm), and some were even smaller than 2 μm (Table S3 in Supplementary Information). No particle size data were available from the natural stone cases for comparison.

**DISCUSSION**

In the present study, we report an outbreak of accelerated silicosis caused by artificial stone dust, which is different from natural stone-associated silicosis. All patients with artificial stone-associated silicosis had performed cutting or polishing without adequate ventilation or respiratory protection, which inevitably leads to high-level exposure to RCS.

In our cohort, the 18 patients diagnosed with artificial stone-associated silicosis had a mean age of 36.1 ± 9.6 years, a median exposure time of 6.1 years and median duration of exposure to artificial stone-associated dust prior to onset of symptoms of 6.4 years. This is significantly shorter than times reported for patients with chronic silicosis caused by exposure in other industries. Previous studies reported durations of occupational exposure to artificial stone-derived silica of 4–10 years. The manifestations of artificial stone-associated silicosis were nodular centrilobular GGO, indistinct boundaries, ground-glass attenuation, a high prevalence of PMF and emphysema. These features differ from those of traditional silicosis nodules, which are usually well circumscribed, round and fairly uniform in size and density. In addition, some, but not all, patients with artificial stone-associated silicosis had mediastinal lymphadenopathy. These HRCT imaging features suggest early-stage silicosis. Rapid radiological progression occurred in 13 patients with artificial stone-associated silicosis over a period of 6–12 months, while no change was found on HRCT in the size, density or distribution of the opacities in 63 patients with natural stone-associated silicosis.

Respiratory function tests in patients with artificial stone-associated silicosis primarily demonstrated restrictive defect patterns and reduced gas transfer, while the respiratory function of patients with natural stone-associated silicosis mainly demonstrated obstructive ventilatory dysfunction. Four patients with artificial stone-associated silicosis experienced rapid deterioration in lung function over the following 6–12 months, with...
In 2016, China reported 10,072 newly diagnosed cases of silicosis, among which 43.78% were concentrated in Sichuan, Hunan and Chongqing provinces and Beijing. However, to our knowledge, there have been no reports of artificial stone-associated silicosis in China until now. The artificial stone industry in China began in the early 2000s, and it is mainly localized in the Pearl River Delta and Yangtze River Delta. The cities of Zhongshan, Heshan and Foshan are the earliest and the largest production areas. The 18 patients we treated for artificial stone-associated silicosis were mainly from these areas. There are currently insufficient epidemiological data on artificial stone-associated silicosis in China; further investigation is required.

Our findings highlight the severity of silicosis associated with artificial stone. More cases are likely to occur unless effective preventive measures are taken and safety practices are enforced. Occupational dust control is one of the key preventative measures against silicosis. The US National Institute of Occupational Safety and Health (NIOSH) recommends limiting exposures to RCS is 0.05 mg/m³. Currently, the RCS exposure standard in China is 0.2 mg/m³ as an 8-h time-weighted average. We recommend strict enforcement in artificial stone production. It is important to frequently monitor RCS exposures to detect overexposures in a timely manner. Collective protective measures should be applied in artificial stone workshops, including both wet cutting and local exhaust ventilation. Workers should be made aware of the risk associated with fabricating and cutting artificial stone. Personal protective equipment such as a protective mask, goggles, gloves, special footwear and a helmet should be used while working. Occupational health surveillance should be conducted regularly to detect silicosis early and intervene to prevent progression by halting further exposure.

Several limitations of this study should be noted. First, our patients were recruited from a single medical centre and the incidence of artificial stone-associated silicosis in other areas of China is as yet unknown. Second, the patients with artificial stone-associated silicosis had been referred from various provinces to our medical centre because we specialize in occupational medicine; thus, there may have been a selection bias. Third, because the study period was recent, the follow-up period was relatively short. Finally, monitoring of workplace exposure was not possible.

In conclusion, artificial stone-associated silicosis is characterized by a shorter latency, rapid radiological progression and accelerated loss of lung function. More individuals who have been exposed to artificial stone dust are likely to be diagnosed as having accelerated silicosis. Urgent action is required to increase awareness of the risk of silicosis in the artificial stone fabrication industry, and measures to control dust levels and monitor and protect workers in this industry are needed.

Acknowledgements: We thank all doctors and nurses from the Department of Occupational Diseases and Clinical Toxicology of Beijing Chao-Yang Hospital for their dedicated efforts in the management of the patients. The work was supported by National Natural Science Foundation of China (81970061) and Application of Clinical Characteristics in Capital (Z181100001718118).

Author contributions: Conceptualization: Q.Y. Data curation: N.W. Formal analysis: N.W. Funding acquisition: Q.Y. Investigation: N.W., C.X., S.Y. Supervision: Q.Y. Writing—original draft: N.W., C.X., S.Y. Writing—review and editing: Q.Y.

Abbreviations: DLCO, diffusing capacity of the lung for carbon monoxide; FEV₁, forced expiratory volume in 1 s; FVC, forced vital capacity; GGO, ground-glass opacity; PMF, progressive massive fibrosis; RCS, respirable crystalline silica.

REFERENCES

1. Scarisbrick D. Silicosis and coal workers’ pneumoconiosis. Practitioner 2002; 246: 117–9.
2. Rimal B, Greenberg AK, Rom WN. Basic pathogenic mechanisms in silicosis: current understanding. Curr. Opin. Pulm. Med. 2005; 11: 169–73.
3. Leung CC, Yu IT, Chen W. Silicosis. Lancet 2012; 379: 2008–18.
4. Hoy RF, Baird T, Hammerschlag G, Hart D, Johnson AR, King P, Putt M, Yateset DH. Artificial stone-associated silicosis: a rapidly emerging occupational lung disease. Occup. Environ. Med. 2018; 75: 3–5.
5. Shtraichman O, Blanc PD, Ollech JE, Fridel L, Fuku L, Fireman E, Kramer MR. Outbreak of autoimmune disease in silicosis linked to artificial stone. Occup. Med. 2015; 65: 444–50.
1. Perez-Alonso A, Cordoba-Doña JA, Millares-Lorenzo JL, Figueroa-Murillo E, García-Vadillo C, Romero-Morill J. Outbreak of silicosis in Spanish quartz conglomerate workers. *Int. J. Occup. Environ. Health* 2014; 20: 26–32.

2. Pascual S, Urrutia I, Ballaz A, Arrizubieta I, Altube L, Salinas C. Prevalence of silicosis in a marble factory after exposure to quartz conglomerates. *Arch. Bronconeumol.* 2011; 47: 50–1.

3. Paolucci V, Romeo R, Sisinni AG, Bartoli D, Mazzei MA, Sartorelli P. Silicosis in workers exposed to artificial quartz conglomerates: does it differ from chronic simple silicosis? *Arch. Bronconeumol.* 2015; 51: e57–60.

4. Pascual DP, García SR, García RM, Barroso ME, Flores RE, Carbonell JG. Silicosis: a former occupational disease with new occupational exposure scenarios. *Rev. Clin. Esp.* 2019; 219: 26–9.

5. Kramer MR, Blanc PD, Fireman E, Amital A, Guber A, Rahaman NA, Shitrit D. Artificial stone silicosis. *Chest* 2012; 142: 419–24.

6. Hering KG, Jacobsen M, Bosch-Galetke E, Elliehausen HJ, Hieckel HG, Hofmann-Preiss K, Jacques W, Jeremie U, Kotschy-Lang N, Kraus T et al. Further development of the International Pneumoconiosis Classification - from ILO 1980 to ILO 2000 and to ILO 2000/German Federal Republic version. *Pneumologie* 2003; 57: 576–84.

7. Ophir N, Shai AB, Alkalay Y, Israeli S, Korenstein R, Kramer MR, Fireman E. Artificial stone dust-induced functional and inflammatory abnormalities in exposed workers monitored quantitatively by biometrics. *ERJ Open Res.* 2016; 2: 86–2015.

8. Martinez C, Prieto A, García L, Quero A, González S, Casan P. Silicosis: a disease with an active present. *Arch. Bronconeumol.* 2010; 46: 97–100.

9. Cooper JH, Johnson DL, Phillips ML. Respirable silica dust suppression during artificial stone countertop cutting. *Ann. Occup. Hyg.* 2015; 59: 122–6.

10. Suganuma N, Kusaka Y, Hering KG, Vehmas T, Kraus T, Arakawa H, Parker JE, Kivisaari L, Letourneau M, Guber A, Ahlbom A, Ghebrehiwet B. Artificial stone silicosis: a former occupational disease with new occupational exposure scenarios. *Rev. Clin. Esp.* 2019; 219: 26–9.

11. Kramer MR, Blanc PD, Fireman E, Amital A, Guber A, Rahaman NA, Shitrit D. Artificial stone silicosis. *Chest* 2012; 142: 419–24.

12. Hering KG, Jacobsen M, Bosch-Galetke E, Elliehausen HJ, Hieckel HG, Hofmann-Preiss K, Jacques W, Jeremie U, Kotschy-Lang N, Kraus T et al. Further development of the International Pneumoconiosis Classification - from ILO 1980 to ILO 2000 and to ILO 2000/German Federal Republic version. *Pneumologie* 2003; 57: 576–84.

13. Ophir N, Shai AB, Alkalay Y, Israeli S, Korenstein R, Kramer MR, Fireman E. Artificial stone dust-induced functional and inflammatory abnormalities in exposed workers monitored quantitatively by biometrics. *ERJ Open Res.* 2016; 2: 86–2015.

14. Martinez C, Prieto A, García L, Quero A, Gonzalez S, Casan P. Silicosis: a disease with an active present. *Arch. Bronconeumol.* 2010; 46: 97–100.

15. Cooper JH, Johnson DL, Phillips ML. Respirable silica dust suppression during artificial stone countertop cutting. *Ann. Occup. Hyg.* 2015; 59: 122–6.

16. Suganuma N, Kusaka Y, Hering KG, Vehmas T, Kraus T, Arakawa H, Parker JE, Kivisaari L, Letourneau M, Guber A, Ahlbom A, Ghebrehiwet B. Artificial stone silicosis: a former occupational disease with new occupational exposure scenarios. *Rev. Clin. Esp.* 2019; 219: 26–9.

17. Kramer MR, Blanc PD, Fireman E, Amital A, Guber A, Rahaman NA, Shitrit D. Artificial stone silicosis: a disease with an active present. *Arch. Bronconeumol.* 2010; 46: 97–100.

18. Cooper JH, Johnson DL, Phillips ML. Respirable silica dust suppression during artificial stone countertop cutting. *Ann. Occup. Hyg.* 2015; 59: 122–6.

19. Blackley DJ, Halldin CN, Cummings KI, Lanev AS. Lung transplantation is increasingly common among patients with coal workers’ pneumoconiosis. *Am. J. Ind. Med.* 2016; 59: 175–7.

20. Ooi GC, Tsang KW, Cheung TF, Khong PL, Ip IW, Ip MS, Tam CM, Ngan H, Lam WK, Chan FL et al. Silicosis in 76 men: qualitative and quantitative CT evaluation – clinical-radiologic correlation study. *Radiology* 2003; 228: 816–25.

21. Takahashi M, Nitta N, Kishimoto T, Ohtsuka Y, Honda S, Ashizawa K. Computed tomography findings of arc-welders’ pneumoconiosis: comparison with silicosis. *Eur. J. Radiol.* 2018; 107: 98–104.

22. Kim JS, Lynch DA. Imaging of nonmalignant occupational lung disease. *J. Thorac. Imaging* 2002; 17: 235–12.

23. Wells AU, Desai SR, Rubens MB, Goh NS, Cramer D, Nicholson AG, Colby TV, du Bois RM, Hansell DM. Idiopathic pulmonary fibrosis: a composite physiologic index derived from disease extent observed by computed tomography. *Am. J. Respir. Crit. Care Med.* 2003; 167: 962–9.

24. López-Llao A, Escrig A, Orts MI, Mallol G, Monfort E. Quartz dustiness: a key factor in controlling exposure to crystalline silica in the workplace. *J. Occup. Environ. Hyg.* 2016; 13: 817–26.

25. Oberdorster G, Ferin J, Lehnerd BE. Correlation between particle size, in vivo particle persistence, and lung injury. *Environ. Health Perspect.* 1994; 102(Suppl. 5): 173–9.

26. Wang J, Fan Y. Lung injury induced by TiO2 nanoparticles depends on their structural features: size, shape, crystal phases, and surface coating. *Int. J. Mol. Sci.* 2014; 15: 22558–78.

27. Leso V, Fontana L, Romano R, Gervetti P, Iavicoli I. Artificial stone associated silicosis: a systematic review. *Int. J. Environ. Res. Public Health* 2019; 16: 568.

28. National Health Commission of the People’s Republic of China. Bulletin on the work of occupational disease prevention and treatment in 2016. [Accessed 20 Dec 2017.] Available from URL: http://www.nhc.gov.cn/zyjks/zcwj2/201712/90667a5571e44ccca42e317b68f50c40.shtml.

29. Laney AS, Weissman DN. Respiratory diseases caused by coal mine dust. *J. Occup. Environ. Med.* 2014; 56(Suppl. 10): S18–22.

30. National Health Commission of the People’s Republic of China. Occupational exposure limits for hazardous agents in the workplace. Part 1: Chemical hazardous agents: GBZ2.1-2007. Beijing: People’s Medical Publishing House, 2007.

### Supplementary Information

Additional supplementary information can be accessed via the html version of this article at the publisher’s website.

**Table S1** An occupational history questionnaire.

**Table S2** Deterioration of lung function in patients with natural stone-associated silicosis.

**Table S3** The size of particulate matter in the four artificial stone samples.

**Visual Abstract** Artificial stone-associated silicosis in China: A prospective comparison with natural stone-associated silicosis.