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Risk of fractures in vitiligo patients treated with phototherapy—A retrospective population-based cohort study

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ABSTRACT

Background: Phototherapy might increase bone mineral density. However, it is unknown whether phototherapy can reduce the risk of fractures in patients with vitiligo.
Objectives: To investigate the effect of phototherapy on fracture risks in vitiligo patients aged 40 or older.
Methods: This population-based cohort study used the 2000–2010 Taiwan National Health Insurance Research Database (NHIRD) to identify 3863 patients newly diagnosed with vitiligo between 2003 and 2009 at age ≥40 years. Study subjects were classified into three cohorts: (1) frequent phototherapy; (2) infrequent phototherapy; and (3) no phototherapy. Patients were followed until the first hip or vertebral fracture or 31 December 2010. Data were analysed using Cox regression models and also stratified by age and gender.
Results: Frequent phototherapy decreased the fracture risks (adjusted hazard ratio (aHR) = 0.32, p = 0.009) in vitiligo patients. Stratification by age and gender confirmed the fracture prevention effect of frequent phototherapy in patients aged 40–64 years (aHR = 0.14, p = 0.016) and in female patients (aHR = 0.31, p = 0.024).
Conclusions: This study provides the first evidence that frequent phototherapy can reduce the risk of fractures among middle-aged and among female vitiligo patients.

1. Introduction

Vitiligo is caused by selective loss of epidermal melanocytes that results in patches of white skin. Worldwide prevalence of vitiligo is 1–2% overall, but this varies between different populations. Those affected can suffer devastating psychological distress [1]. Vitiligo affects women younger and more prevalent than men, which may reflect an aetiologic association with underlying autoimmune dysregulation to which females are more susceptible, or, indirectly, greater concerns to the negative effect on the appearance [1].

Diverse mechanisms that may contribute to the aetiology of vitiligo have been proposed; these include autoimmune, genetic, biochemical, oxidative stress, neural, and viral factors [2]. Vitiligo has also been associated with other autoimmune diseases, for example, autoimmune thyroid disease, rheumatoid arthritis,

Abbreviations: aHR, adjusted hazard ratio; CI, confidence interval; DDD, defined daily dose; HR, hazard ratio; ICD-9-CM, International Classification of Disease, Ninth Revision, Clinical Modification; NHI, National Health Insurance; NHIRD, National Health Insurance Research Database; SD, standard deviation.

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diabetes mellitus, psoriasis, and lupus erythematosus, among others [3,4]. Notably some such vitiligo-associated diseases, for instance, rheumatoid arthritis, are also potential risk factors for osteoporosis and fractures [5–7].

Various treatment options that have been used include topical corticosteroids, calcineurin inhibitors, vitamin D_3 analogues (calcipotriene), systemic steroid, anti-oxidants, phototherapy, and surgery [2]. Topical calcineurin inhibitors and topical corticosteroids are the common first-line therapy, with phototherapy, particularly narrowband ultraviolet light B, reserved as second-line therapy for patients with extensive vitiliginous lesions or lesions on exposed areas after first-line therapy fails [8].

Some studies have found vitiligo patients to have lower serum vitamin D levels; however, this remains controversial [9,10]. Others have reported increased serum vitamin D in vitiligo patients treated with phototherapy [11]. Since vitamin D plays a significant role in calcium and bone mineral metabolism [12], it is rational to hypothesize that vitiligo patients treated with phototherapy may have a reduced risk of fractures, consequent to elevated vitamin D levels. Although previous studies have reported increased serum 25-hydroxyvitamin D_3 synthesis and bone mineral density in elderly psoriatic women treated with phototherapy [13,14], none have investigated whether phototherapy could actually reduce fracture risks. Therefore, we conducted a retrospective population-based cohort study to analyse the incidence of primary hip or vertebral fracture among vitiligo patients aged 40 years or older and to determine whether phototherapy can reduce their risk of fractures.

2. Materials and methods

2.1. Study design

We classified eligible patients into three cohorts, based on the frequency of phototherapy (Fig. 1), and follow up their outcome. We defined frequency of phototherapy as the accumulated times of phototherapy divided by follow-up period. This "average" frequency of phototherapy was used because the patients had heterogeneous observational period, from one year to eight years. A frequent phototherapy cohort comprised patients who received phototherapy (national reimbursement codes, phototherapy: 51019B) at least 24 times per year on average; those who received phototherapy between 1 and 23 times per year on average comprised the infrequent phototherapy cohort; the control cohort received no phototherapy. We defined receiving at least 24 times of phototherapy per year on average as frequent phototherapy since Bogh et al.'s study indicated that ultraviolet B exposure of 1 standard erythema dose every second week is sufficient for maintaining summer vitamin D levels during the winter [15]. This operational definition resulted in a frequent phototherapy cohort receiving more phototherapies than Bogh et al. suggested (a ultraviolet B dose every second week), theoretically. The reimbursement code of phototherapy (51019B) in the NHIRD dataset covers mainly narrowband UVB, and does not cover PUVA, lower level laser, and excimer laser therapy.

The entry date for each cohort was the first date of vitiligo diagnosis. Subjects were followed-up until an incident of (new) hip or vertebral fracture, withdrawal from the NHI program, or 31 December 2010, whichever came first. Fig. 2 shows the study design.

2.2. Data source

All data were obtained from the Taiwan National Health Insurance (NHI) Research Database (NHIRD) from 2000 to 2010. The Taiwan NHI program covers 99% of the Taiwan population and offers comprehensive medical care to beneficiaries – the NHIRD, which has been described in detail elsewhere [16–18], stores their medical records and demographic data. This research used a specific NHIRD subject dataset that contains all patients in Taiwan diagnosed with vitiligo from 2000 to 2010. This study was exempt from full review by an Institutional Review Board because the NHIRD consists of de-identified secondary data made available for research.

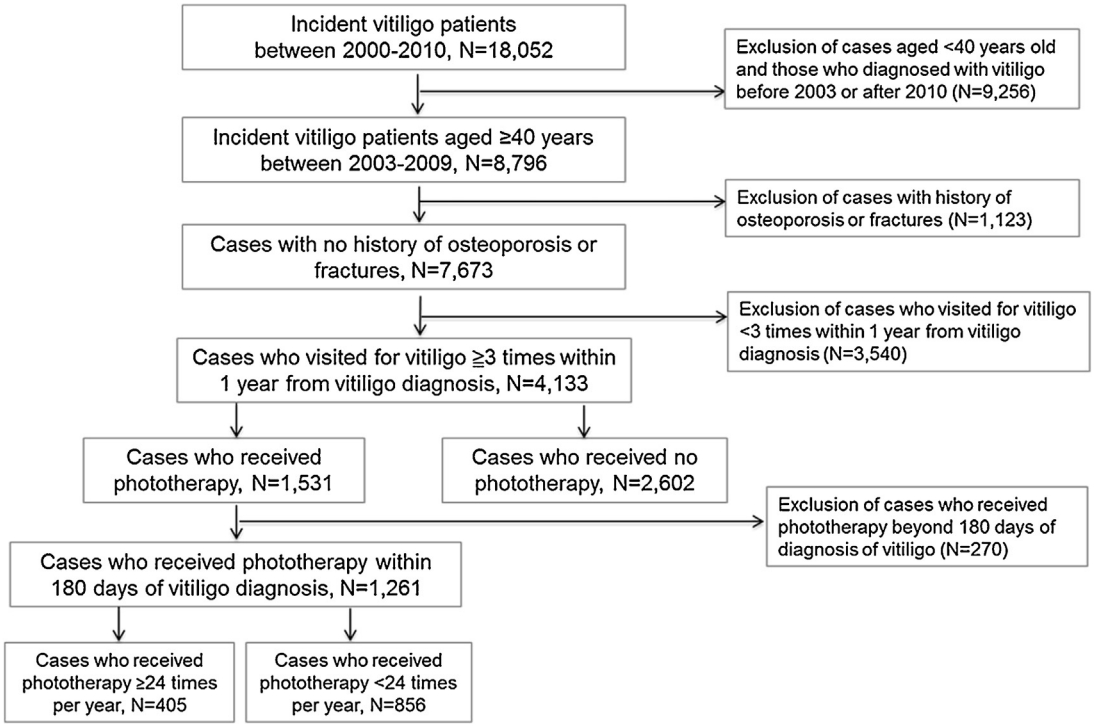

Fig. 1. Flowchart of study cohort selection.