Ann Dermatol Vol. 33, No. 3, 2021
pISSN 1013-9087 · eISSN 2005-3894
https://doi.org/10.5021/ad.2021.33.3.203

ORIGINAL ARTICLE

Association of Metabolic Comorbidities with Pediatric Psoriasis: A Systematic Review and Meta-Analysis

Soo Ick Cho*, Ye Eun Kim*, Seong Jin Jo

Department of Dermatology, Seoul National University College of Medicine, Seoul, Korea

Background: An evident relationship has been shown between psoriasis and metabolic comorbidities. However, the results in pediatric psoriasis vary from study to study, and no meta-analysis exists on the association of metabolic comorbidities with pediatric psoriasis. **Objective:** To evaluate the association between psoriasis and metabolic comorbidities in pediatric patients. **Methods:** We searched articles published in PubMed, EMBASE, and Cochrane Library databases from inception to April 30, 2019. All observational studies reporting the prevalence of obesity or metabolic comorbidities in pediatric patients with psoriasis were included. **Results:** The meta-analysis included 16 unique studies meeting the inclusion criteria. The pooled odds ratios in pediatric patients with psoriasis was 2.40 (95% confidence interval [CI], 1.60～3.59) for obesity (13 studies), 2.73 (95% CI, 1.79～4.17) for hypertension (8 studies), 2.01 (95% CI, 1.09～3.73) for diabetes mellitus (8 studies), 1.67 (95% CI, 1.42～1.97) for dyslipidemia (7 studies), and 7.49 (95% CI, 1.86～30.07) for metabolic syndrome (4 studies). **Conclusion:** Pediatric patients with psoriasis showed a significantly higher prevalence of obesity, hypertension, diabetes, dyslipidemia, and metabolic syndrome. Adequate monitoring and timely management of metabolic comorbidities should be considered in these patients. **(Ann Dermatol 33(3) 203～213, 2021)**

-Keywords-
Diabetes mellitus, Hypertension, Metabolic syndrome, Obesity, Psoriasis

INTRODUCTION

Psoriasis is one of the most common chronic inflammatory skin diseases with a prevalence of approximately up to 2% in adolescents[1]. Recent studies have suggested that psoriasis is not just an inflammatory skin disease, but it is associated with various systemic diseases[2]. Increased risk of cardiovascular outcome and metabolic comorbidities, such as diabetes, hypertension, and obesity, has been observed in patients with psoriasis[3-5]. Metabolic comorbidity, among several comorbid diseases, is common in developed countries and can be managed through proper lifestyle modification and treatment. Uncontrolled metabolic comorbidity increases mortality by inducing cardiovascular disease[6].

The prevalence of psoriasis in children is known to be lower than that in adults[1,7]. The prevalence of metabolic comorbidities in children is also low; therefore, accompanying metabolic comorbidities in pediatric psoriasis are easily overlooked. However, the prevalence of psoriasis was reported to increase in adolescence, which is an important period for managing metabolic comorbidities[8-10].

Several studies observed higher risk of metabolic comorbidities in pediatric groups with psoriasis than in control groups[11-13] In this regard, active screening for metabolic comorbidities in pediatric patients with psoriasis is recommended, but the level of evidence is low[14]. Meta-analyses of studies about the association between adult psoriasis and obesity, hypertension, diabetes, dyslipidemia, and

Received June 9, 2020, Revised September 20, 2020, Accepted for publication October 5, 2020

*These authors have equally contributed to the article.

Corresponding author: Seong Jin Jo, Department of Dermatology, Seoul National University College of Medicine, 103 Daehak-ro, Jongno-gu, Seoul 03080, Korea. Tel: 82-2-2072-4916, Fax: 82-2-742-7344, E-mail: sj.jo@snu.ac.kr
ORCID: https://orcid.org/0000-0002-2501-7672

metabolic syndrome were performed and confirmed the significant association[15-19], but meta-analysis about the association between pediatric psoriasis and the aforementioned comorbidities has not been performed. In this study, we performed a meta-analysis to evaluate the association of metabolic syndrome including obesity, diabetes, hypertension, and dyslipidemia with psoriasis in pediatric patients.

MATERIALS AND METHODS

This study received an exemption determination from the institutional review board of Seoul National University Hospital (no. 2104-166-1214). Following the Meta-analysis of Observational studies in Epidemiology (MOOSE) guideline, meta-analysis of observational case-control studies, excluding cohort studies, about the prevalence of metabolic comorbidity in pediatric psoriasis was performed[20].

Study search and selection

Articles published in PubMed, EMBASE, and Cochrane Library databases from inception to April 30, 2019 were searched. The search was conducted using MeSH terms and free text keywords related to "pediatric," "psoriasis," "obesity," "hypertension," "diabetes," "dyslipidemia," and "metabolic syndrome" (Supplementary Table 1). Reference lists of searched articles were also reviewed.

After excluding duplicate articles, two authors (YEK and SIC) independently screened the title and abstract of articles. Full text was reviewed for articles with title and abstract only which made difficult to evaluate eligibility. Population under 19 years of age (≤18 years of age) was defined as pediatric population. Observational studies, including cross-sectional, case-control, and cohort studies, were included. Studies meeting the following inclusion criteria were finally selected: (1) studies with at least 10 patients with psoriasis vulgaris aged 18 years or below, (2) studies with control group originated from the same database and with at least 10 control subjects, (3) studies measured outcomes for obesity, hypertension, diabetes, dyslipidemia, and/or metabolic syndrome (other outcomes such as overweight, high blood pressure, or insulin resistance were not included), (4) studies with observation period limited to 18 years old or below, and (5) English-written original articles or research letters with adequate information. Studies with more than half of patients have psoriatic arthritis or unable to separate psoriasis vulgaris, only the patient group was excluded. For relevant unpublished studies (studies with abstract only), we attempted to contact with author through e-mail, but studies without sufficient information were excluded.

The Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) diagram of the search and selection of studies is presented in Fig. 1.

Data extraction and study quality assessment

The following information was extracted from articles by two authors (YEK and SIC).

- General data: First author, year of publication, country, age range, number of cases/controls included, study design
- For comorbidity evaluation: definition of comorbidity, prevalence of obesity/hypertension/diabetes mellitus/hyperlipidemia/metabolic syndrome and information needed to calculate prevalence of obesity/hypertension/diabetes mellitus/hyperlipidemia/metabolic syndrome

The quality of the included studies was assessed by two authors (YEK and SIC) using the Newcastle-Ottawa scale modified by Miller et al.[21] (score range 0～11). This scale includes selection (case definition, representativeness of the cases, selection of controls, and definition of controls), comparability, and methods. Publication bias of the included studies was evaluated by visual inspection of funnel plot and Egger's regression test[22].

Statistical analysis

Statistical analysis was performed using "meta" package of R version 3.5.0 (R Foundation for Statistical Computing, Vienna, Austria) statistical software. Random effect model was used to calculate pooled odds ratio (OR) with 95% confidence interval (CI). Study heterogeneity was assessed using Cochran's Q test and I^2 index. The result with *p*-value >0.1 from Cochran's Q test or I^2 index >75 was considered having substantial heterogeneity and random effect model was applied.

RESULTS

Study selection

A total of 4,532 studies were identified through database search. After excluding 668 duplicate articles and 3,728 inappropriate articles through title and abstract screening, 136 articles were full text reviewed. Articles were excluded for the following reasons: no pediatric data or undistinguishable pediatric data (n=72), no prevalence data (n=7), no detailed data (n=2), no or inappropriate control (n=6), duplicate data source (n=1), studies for psoriatic arthritis (n=2), inappropriate outcome (n=8), inappropriate study design (n=13), and full text unavailable (n=8). A total of 17 studies[11-13,23-36] met the eligibility criteria; 15 were case-control or cross-sectional studies1[1-13,23-30,32-35], one was a cohort study[36], and one study included both case-control and cohort data[31]. Meta-analysis for case-con-

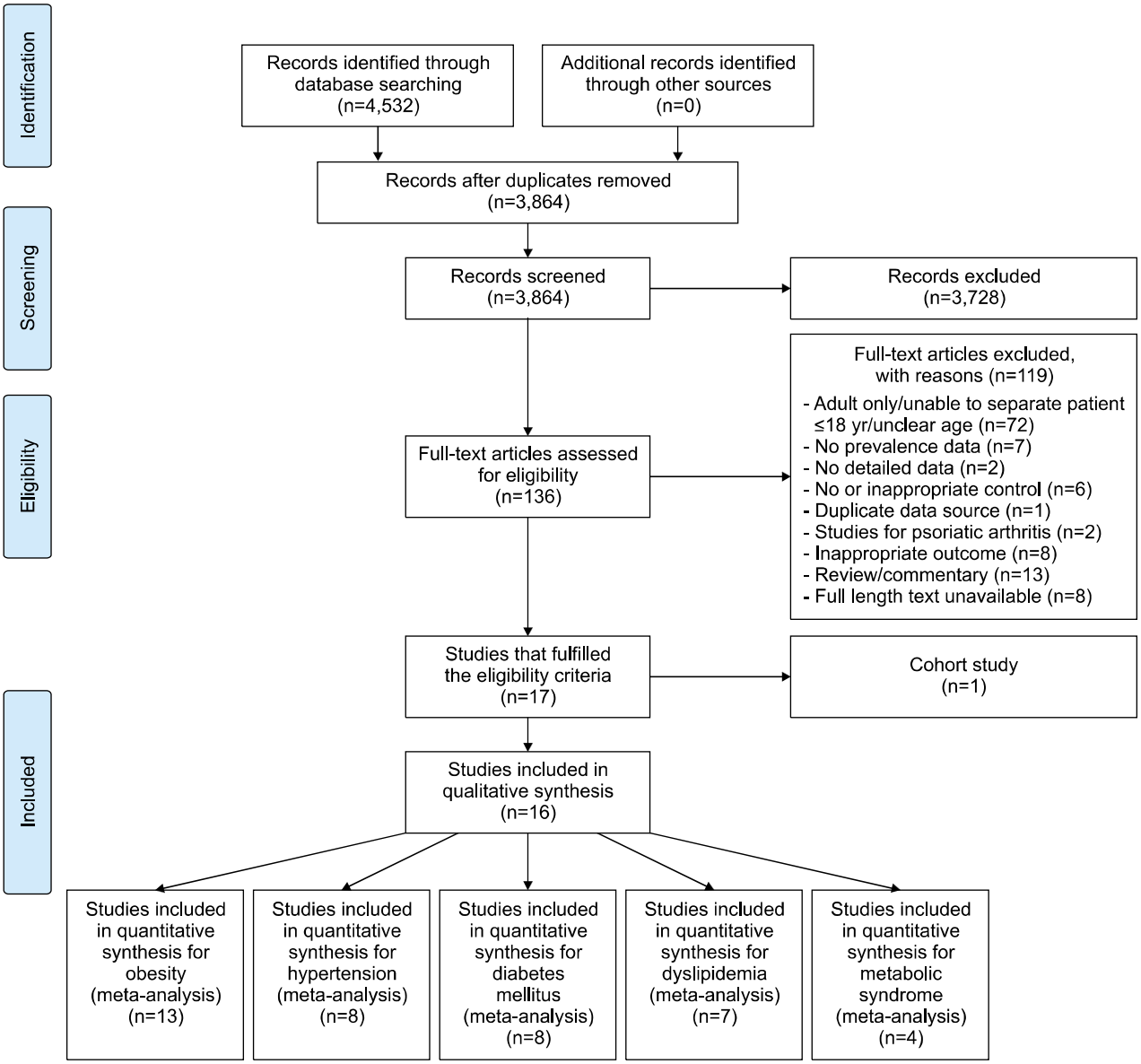

Fig. 1. Flowchart of study selection following the PRISMA guideline.

trol or cross-sectional studies and cohort studies should be performed separately because the outcomes of each are different (prevalence vs. incidence). However, we could not perform meta-analysis for cohort studies because only two met our eligibility criteria. Moreover, some participants in these cohort studies may have become adults during the follow-up period. Finally, 16 studies[11-13,23-35] with 20,676 psoriasis cases and 5,239,197 controls were included for meta-analysis.

Description of the included studies

Characteristics of included studies are summarized in Supplementary Table 2. A total of six studies[11,26,29,31,32,35] were from the United States, followed by five studies[12,13,25,30,33] from Europe (including France, Germany, Italy, Portugal, and Turkey). All studies were published after 2008. All studies included patients aged 5 to 14 years, and studies including patients aged 0 to 18 years were the most common (n=4)[11,26,30,31]. The design of the 13 studies[11,12,23-28,30-33,35] was case-control, and that of the other three studies[13,29,34] was cross-sectional. For data source, 10 studies[12,23-28,30,33,35] recruited the participants at medical institutions, and the other six studies[11,13,29,31,32,34] utilized electronic health record databases. Twelve studies[11,13,25-32,34,35] included patients with psoriasis, and the other four studies[12,23,24,33] included patients with plaque psoriasis. One study[12] excluded patients with psoriatic arthritis. Two studies[12,31] included all five clinical outcomes, and five studies[11,13,25,29,32]

included the outcome of obesity, hypertension, diabetes mellitus, and dyslipidemia. One study[27] reported the outcome of obesity and metabolic syndrome. Eight studies showed single outcome including obesity (n=5)[23,24,26,28,30], diabetes mellitus, hypertension, and metabolic syndrome (n=1, in each)[33-35]. Half of the included studies[11,25,26,30-33,35] showed high quality with ≥9 points, and the other half of the included studies[12,13,23,24,27-29,34] showed middle quality with 6 to 8 points according to the modified version of the Newcastle-Ottawa scale (Supplementary Table 3).

Association of pediatric psoriasis and obesity

A total of 13 studies[11-13,23-32] (20,019 psoriasis cases and 5,219,428 controls) about the prevalence of obesity were identified. Four studies[11,13,29,32] defined obesity according to the diagnostic code, and nine studies[12,23-28,30,31] defined

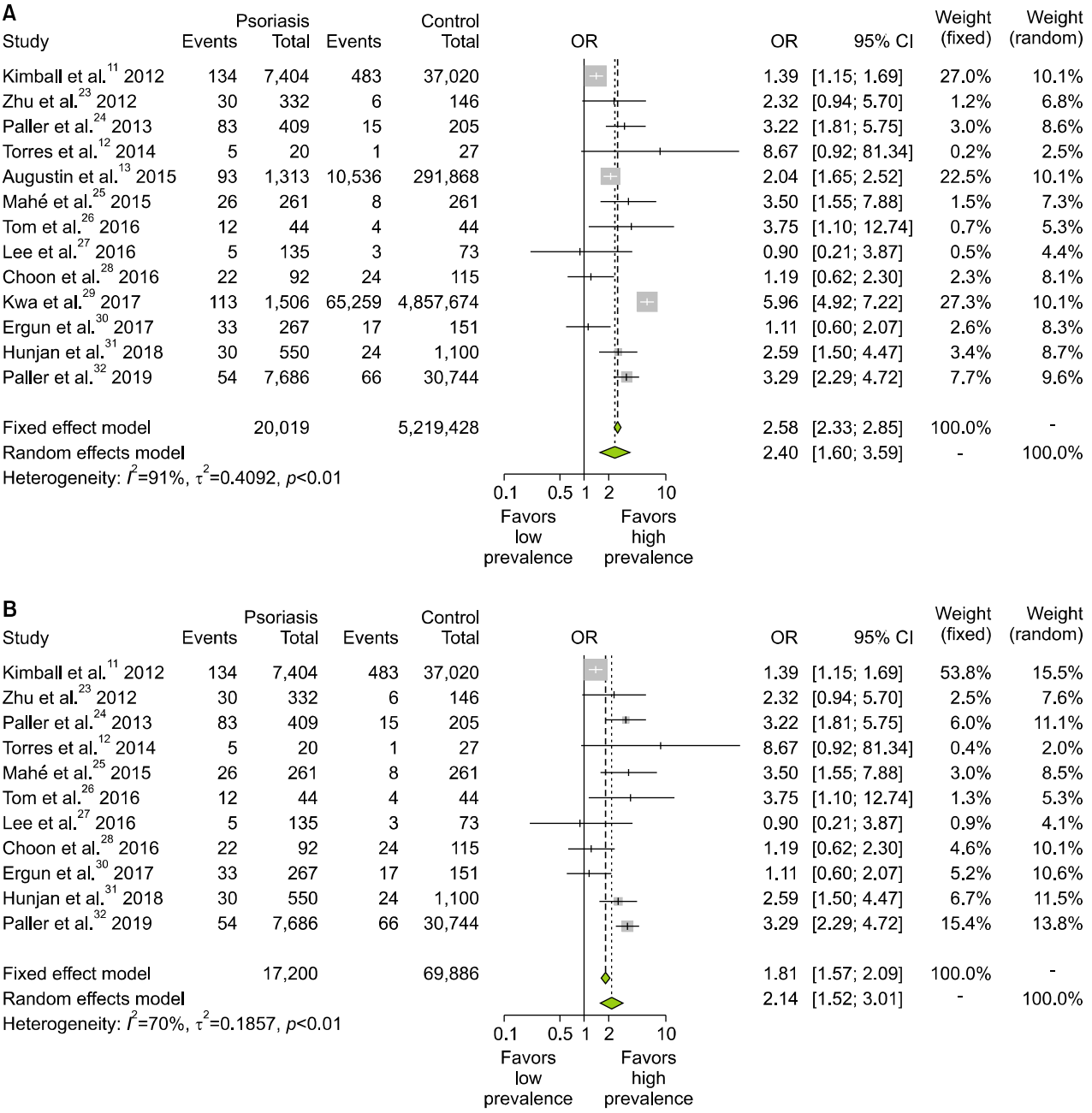

Fig. 2. Association of pediatric psoriasis with obesity. (A) Quantitative analysis of all 13 articles about the association between pediatric psoriasis and obesity. (B) Quantitative analysis of 11 articles with case-control design. (C) Quantitative analysis of nine articles that defined obesity by body mass index. (D) Quantitative analysis of six articles that defined obesity as body mass index ≥95 percentile. OR: odds ratio, CI: confidence interval.

obesity clinically including six studies[12,24,26-28,30] that defined obesity by body mass index ≥95 percentile. Quantitative analysis of 13 articles showed significantly higher odds of obesity in children with psoriasis (pooled OR, 2.40; 95% CI, 1.60～3.59) (Fig. 2A). A random-effects model was applied because a substantial heterogeneity was observed among the 13 articles. Subgroup analysis according to the study design and obesity definition was performed. In 11 studies[11,12,23-28,30-32] with case-control study design (17,200 psoriasis cases and 69,886 controls), the odds of obesity were significantly increased in children with psoriasis (pooled OR, 2.14; 95% CI, 1.52～3.01) (Fig. 2B). In nine studies[12,23-28,30,31] that clinically defined obesity (2,110 psoriasis cases and 2,122 controls), significantly increased odds of obesity was observed in children with psoriasis (pooled OR, 2.16; 95% CI, 1.48～3.13) (Fig. 2C). In 6 studies[12,24,26-28,30] that defined obesity as body mass index ≥95 percentile (967 psoriasis cases and 615 controls), significantly increased odds of obesity was observed in children with psoriasis (pooled OR, 1.88; 95% CI, 1.06～3.33) (Fig. 2D).

Association of pediatric psoriasis and metabolic comorbidities

A total of eight studies[11-13,25,29,31-33] (18,792 psoriasis cases and 5,218,746 controls) about the prevalence of hypertension were identified. Quantitative analysis of these studies showed that children with psoriasis have significantly increased odds of hypertension (pooled OR, 2.73; 95% CI, 1.79～4.17) (Fig. 3A). Eight studies[11-13,25,29,31,32,34] (19,325 psoriasis cases and 5,238,391 controls) about the prevalence of diabetes mellitus were identified. Quantitative analysis of these eight studies showed that children with psoriasis have significantly increased odds of diabetes mellitus (pooled OR, 2.01; 95% CI, 1.09～3.73) (Fig. 3B). Seven studies[11-13,25,29,31,32] (18,740 psoriasis cases and

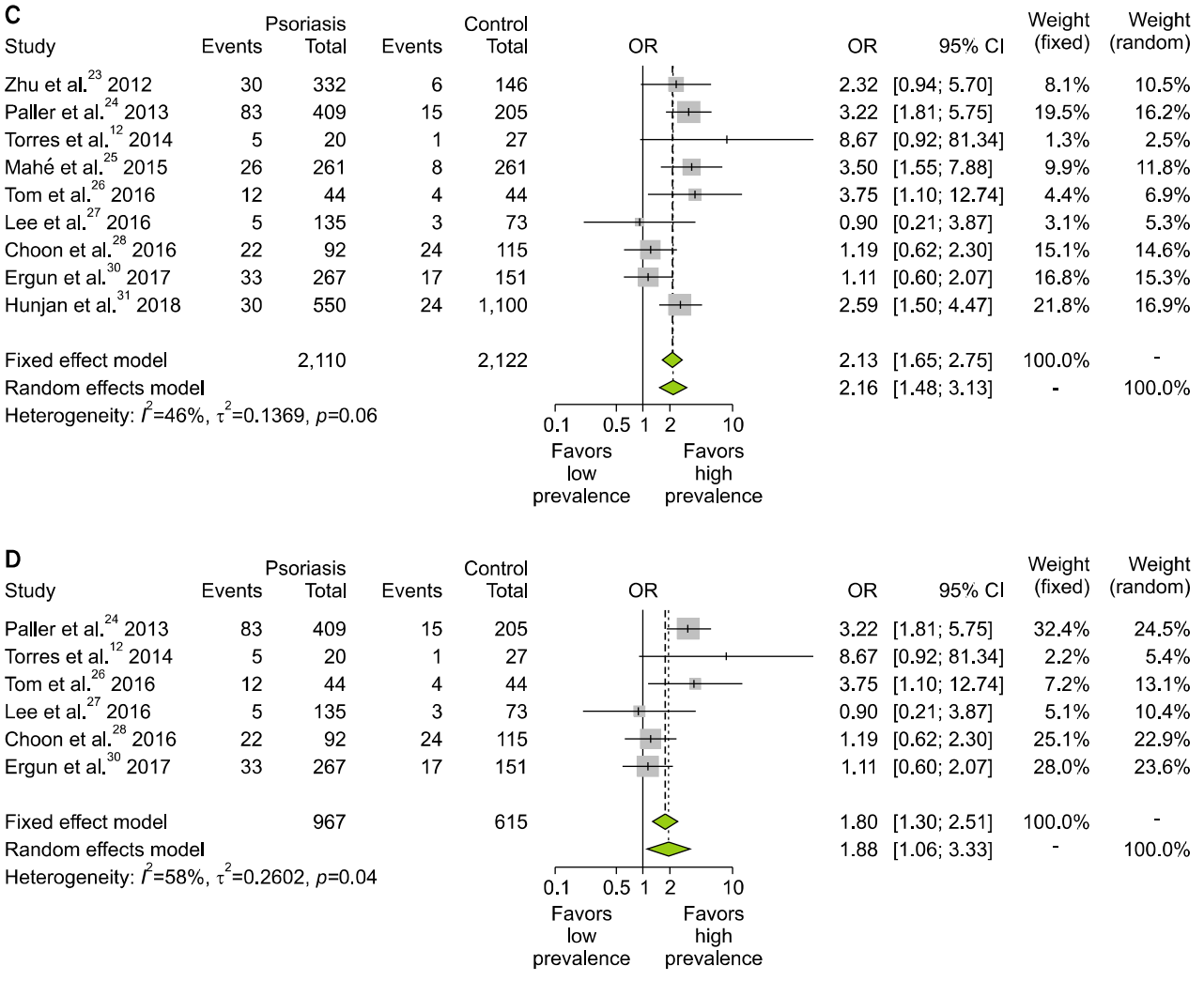

Fig. 2. Continued.

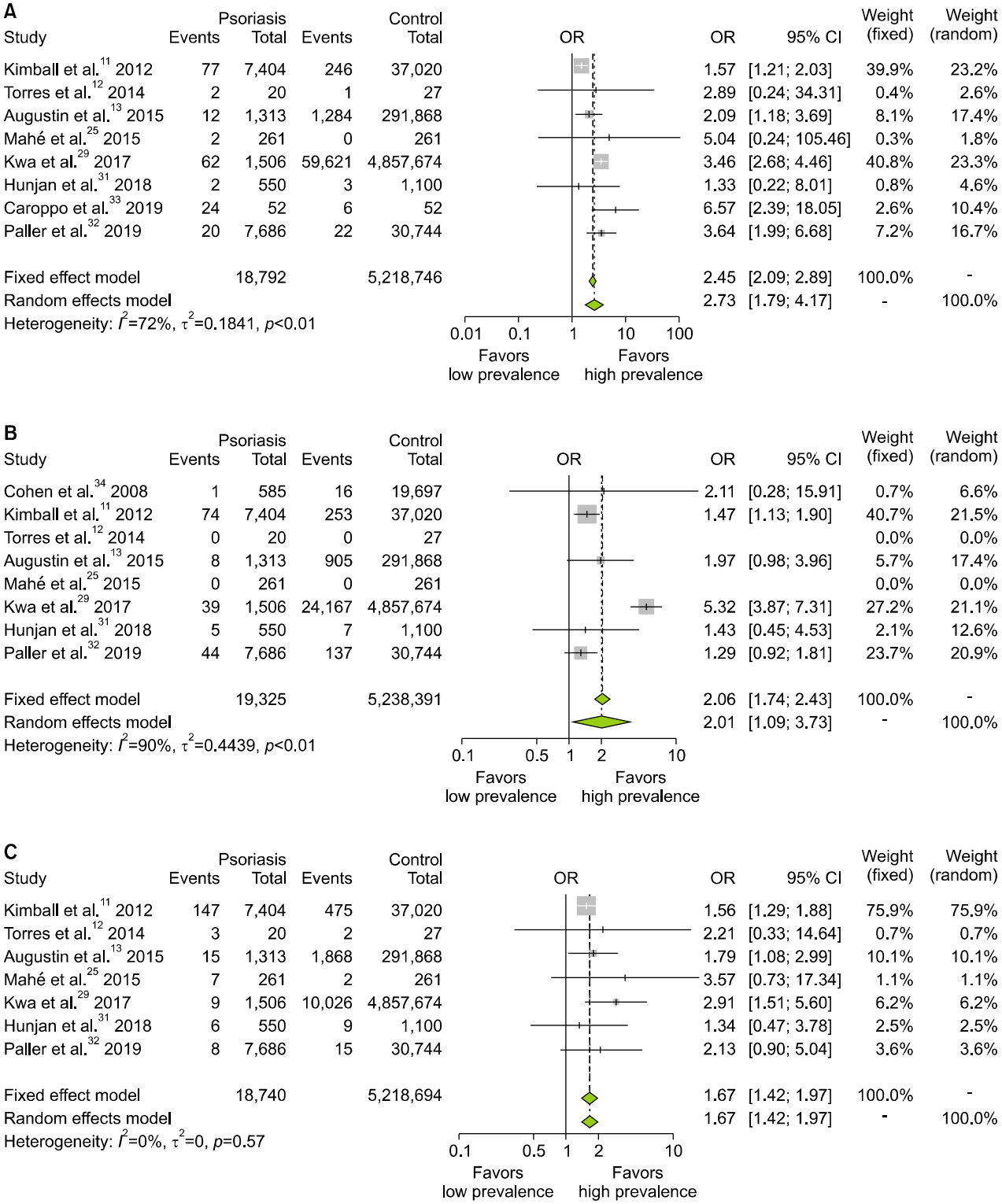

Fig. 3. Association of pediatric psoriasis with metabolic comorbidities. (A) Quantitative analysis of eight articles about the association between pediatric psoriasis and hypertension. (B) Quantitative analysis of eight articles about the association between pediatric psoriasis and diabetes mellitus. (C) Quantitative analysis of seven articles about the association between pediatric psoriasis and dyslipidemia. (D) Quantitative analysis of four articles about the association between pediatric psoriasis and metabolic syndrome. CI: confidence interval.

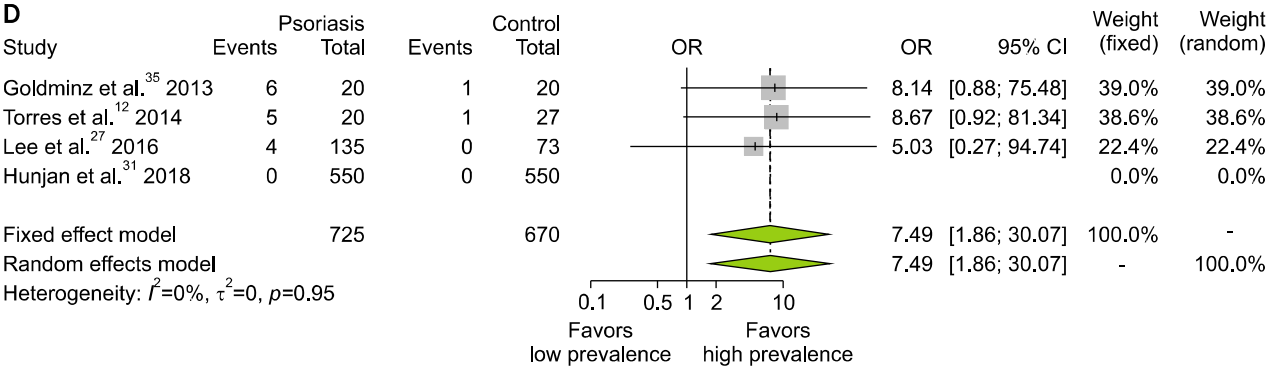

Fig. 3. Continued.

5,218,694 controls) about the prevalence of dyslipidemia were identified. Quantitative analysis of these studies showed that children with psoriasis have significantly higher odds of dyslipidemia (pooled OR, 1.67; 95% CI, 1.42～1.97) (Fig. 3C). Four studies[12,27,31,35] (725 psoriasis cases and 670 controls) about the prevalence of metabolic syndrome were identified. Two studies[12,35] followed the criteria by de Ferranti et al.[37], while one study[27] followed the criteria by the International Diabetes Federation[38]. Quantitative analysis of these studies showed that children with psoriasis have significantly higher odds of metabolic syndrome (pooled OR, 7.49; 95% CI, 1.86～30.07) (Fig. 3D).

Assessment of publication bias

Funnel plot for studies about hypertension, diabetes, dyslipidemia, metabolic syndrome, and obesity showed no evident asymmetry (Supplementary Fig. 1, 2). Egger's regression test also suggested no significant publication bias ($p>0.05$).

DISCUSSION

To our knowledge, this is the first meta-analysis on the association between pediatric psoriasis and metabolic comorbidities. This meta-analysis showed that pediatric patients with psoriasis had significantly higher prevalence of obesity, hypertension, diabetes, dyslipidemia, and metabolic syndrome. In addition, significantly increased prevalence of obesity was observed in children with psoriasis regardless of the definition of obesity.

The association of psoriasis with metabolic comorbidities is well reported in adults. Several studies showed strong association of psoriasis with obesity, hypertension, diabetes, dyslipidemia, and metabolic syndrome[16-19,39,40]. The underlying mechanism of the association between psoriasis and metabolic syndrome is not completely elucidated, but various factors contribute to the association[41]. Genetic relationship between psoriasis and metabolic comorbidities has also been reported[40,42]. In addition, the concept of "psoriatic march" has been proposed, which means expansion of inflammation from skin to systemic[43]. The "psoriatic march" hypothesis suggests that locally overproduced pro-inflammatory cytokines in psoriasis lesion are released into the circulatory system and therefore induce systemic resistance, endothelial dysfunction, oxidative stress, and eventually metabolic comorbidities[41,43]. In cases of psoriasis with metabolic comorbidities, proper management and treatment of metabolic comorbidities are crucial to prevent cardiovascular events, the major complication[21,44,45]. In addition, obesity itself is able to increase the risk and the severity of psoriasis or reduce the psoriasis treatment response, so it should be managed properly[46-48]. Most previous studies, however, are targeted to adults, and studies for children are not sufficient.

Psoriasis in children and adolescents is not uncommon, and a large number of patients with psoriasis who developed psoriasis during childhood experience psoriasis until adulthood[1,7,49]. As in adults, metabolic comorbidities, such as hypertension, diabetes, dyslipidemia, obesity, and metabolic syndrome, were reported to be increased in pediatric patients with psoriasis[7,50,51]. The association between pediatric psoriasis and obesity was reported from a previous systematic review. In this study, the association between obesity and psoriasis in adolescents was consistently observed under various definitions of obesity. The associations of pediatric psoriasis with other metabolic comorbidities were not as much clear as that with obesity in all studies[50,51]. Due to the lower prevalence and under-diagnosis of metabolic comorbidities in pediatric population, individual study, particularly about relatively small population, failed to show significant association between metabolic comorbidities and psoriasis[50,52,53]. However, although not included in the present study, a retrospective cohort study of 29,957 pediatric psoriasis patients re-

ported a significantly higher hazard ratio of hypertension, diabetes, metabolic syndrome, and elevated lipid levels in those patients during the follow-up period[36]. The risk of metabolic comorbidities was significant independent of obesity[36]. Taken together with the result of this meta-analysis, the association between metabolic comorbidities and pediatric psoriasis is clear.

Obesity and metabolic comorbidities in childhood have a poor prognosis with multiple complications including cardiovascular disease in adulthood[54-58]. In pediatric patients with psoriasis, lipid profile associated with high cardiovascular risks was observed, and increased cardiovascular comorbidities were reported but the frequency is not high[26,29]. Since timely treatment and care of metabolic comorbidities and obesity can reduce the risk of complications, active detection and management of high-risk groups for obesity and metabolic comorbidities among pediatric patients with psoriasis are important[14,59-61]. Moreover, treatment with tumor necrosis factor-α inhibitor, interleukin (IL)-12/23 inhibitor, or IL-17 inhibitor was reported to be able to lower the risk of cardiovascular disease in adults; thus, using biologics to pediatric patients with severe psoriasis with metabolic syndrome should be considered[62-65]. Osier et al.[14] proposed an expert consensus recommendation on comorbidity screening guideline in pediatric psoriasis based on studies published up to December 2015 and suggested routine screening for related comorbidities and risk factors identification in pediatric patients with psoriasis. However, evidence level in the study was relative low (Strength of Recommendation Taxonomy level C), and no guideline for management in those patients with metabolic comorbidity was provided. Taken together, further evidence-based guidelines are required to provide adequate metabolic comorbidities screening and management for adolescent patients with psoriasis.

This study has several limitations. First, a total of 16 studies were included in this meta-analysis, but meta-analysis of metabolic comorbidities other than obesity includes less than 10 studies each, which is not adequate. Second, substantial study heterogeneity was observed among the studies. The heterogeneity may result from the difference of each study in subject age, location, severity of psoriasis, and diagnosis criteria of psoriasis, whether diagnosed by dermatologists, medical record, or claims data. For obesity, subgroup analysis was performed according to the study design and diagnosis criteria. In case of other metabolic comorbidities, however, subgroup analysis could not be conducted due to the low number of included studies. Third, there are potential risk of bias such as selection bias and publication bias. Although funnel plot and Egger's regression test suggested no substantial publication bias, potential publication bias cannot be ruled out because of the small number of studies. Finally, this study including only observational studies did not show causality, but only showed the association between psoriasis and metabolic comorbidities. Despite these limitations, this study has significance as the first to present the results of a meta-analysis on the association between pediatric psoriasis and metabolic comorbidities.

This meta-analysis shows that pediatric patients with psoriasis have significantly higher association with obesity, hypertension, diabetes, dyslipidemia, and metabolic syndrome. Dermatologists and pediatricians should be aware of the evident association of metabolic comorbidities with psoriasis in children and should perform early proper investigation and management to prevent disease progress and complications. Further investigations on the casual-relationship and mechanism of the association between pediatric psoriasis and metabolic comorbidities are warranted.

SUPPLEMENTARY MATERIALS

Supplementary data can be found via http://anndermatol.org/src/sm/ad-33-203-s001.pdf.

CONFLICTS OF INTEREST

The authors have nothing to disclose.

FUNDING SOURCE

None.

DATA SHARING STATEMENT

Research data are not shared.

ORCID

Soo Ick Cho, https://orcid.org/0000-0003-3414-9869
Ye Eun Kim, https://orcid.org/0000-0001-6634-5237
Seong Jin Jo, https://orcid.org/0000-0002-2501-7672

REFERENCES

1. Parisi R, Symmons DP, Griffiths CE, Ashcroft DM; Identification and Management of Psoriasis and Associated ComorbidiTy (IMPACT) project team. Global epidemiology of psoriasis: a systematic review of incidence and prevalence. J Invest Dermatol 2013;133:377-385.
2. Yeung H, Takeshita J, Mehta NN, Kimmel SE, Ogdie A, Margolis DJ, et al. Psoriasis severity and the prevalence of major medical comorbidity: a population-based study. JAMA

Dermatol 2013;149:1173-1179.
3. Brauchli YB, Jick SS, Meier CR. Psoriasis and the risk of incident diabetes mellitus: a population-based study. Br J Dermatol 2008;159:1331-1337.
4. Brauchli YB, Jick SS, Miret M, Meier CR. Psoriasis and risk of incident myocardial infarction, stroke or transient ischaemic attack: an inception cohort study with a nested case-control analysis. Br J Dermatol 2009;160:1048-1056.
5. Baeta IG, Bittencourt FV, Gontijo B, Goulart EM. Comorbidities and cardiovascular risk factors in patients with psoriasis. An Bras Dermatol 2014;89:735-744.
6. Obunai K, Jani S, Dangas GD. Cardiovascular morbidity and mortality of the metabolic syndrome. Med Clin North Am 2007;91:1169-1184, x.
7. Burden-Teh E, Thomas KS, Ratib S, Grindlay D, Adaji E, Murphy R. The epidemiology of childhood psoriasis: a scoping review. Br J Dermatol 2016;174:1242-1257.
8. Horton DB, Scott FI, Haynes K, Putt ME, Rose CD, Lewis JD, et al. Antibiotic exposure, infection, and the development of pediatric psoriasis: a nested case-control study. JAMA Dermatol 2016;152:191-199.
9. US Preventive Services Task Force, Grossman DC, Bibbins-Domingo K, Curry SJ, Barry MJ, Davidson KW, et al. Screening for obesity in children and adolescents: US Preventive Services Task Force recommendation statement. JAMA 2017;317:2417-2426.
10. Halpern A, Mancini MC, Magalhães ME, Fisberg M, Radominski R, Bertolami MC, et al. Metabolic syndrome, dyslipidemia, hypertension and type 2 diabetes in youth: from diagnosis to treatment. Diabetol Metab Syndr 2010;2:55.
11. Kimball AB, Wu EQ, Guérin A, Yu AP, Tsaneva M, Gupta SR, et al. Risks of developing psychiatric disorders in pediatric patients with psoriasis. J Am Acad Dermatol 2012;67:651-657.e2.
12. Torres T, Machado S, Mendonça D, Selores M. Cardiovascular comorbidities in childhood psoriasis. Eur J Dermatol 2014;24:229-235.
13. Augustin M, Radtke MA, Glaeske G, Reich K, Christophers E, Schaefer I, et al. Epidemiology and comorbidity in children with psoriasis and atopic eczema. Dermatology 2015;231:35-40.
14. Osier E, Wang AS, Tollefson MM, Cordoro KM, Daniels SR, Eichenfield A, et al. Pediatric psoriasis comorbidity screening guidelines. JAMA Dermatol 2017;153:698-704.
15. Takeshita J, Grewal S, Langan SM, Mehta NN, Ogdie A, Van Voorhees AS, et al. Psoriasis and comorbid diseases: epidemiology. J Am Acad Dermatol 2017;76:377-390.
16. Armstrong AW, Harskamp CT, Armstrong EJ. The association between psoriasis and obesity: a systematic review and meta-analysis of observational studies. Nutr Diabetes 2012;2:e54.
17. Armstrong AW, Harskamp CT, Armstrong EJ. The association between psoriasis and hypertension: a systematic review and meta-analysis of observational studies. J Hypertens 2013;31:433-442; discussion 442-443.
18. Armstrong AW, Harskamp CT, Armstrong EJ. Psoriasis and the risk of diabetes mellitus: a systematic review and meta-analysis. JAMA Dermatol 2013;149:84-91.
19. Armstrong AW, Harskamp CT, Armstrong EJ. Psoriasis and metabolic syndrome: a systematic review and meta-analysis of observational studies. J Am Acad Dermatol 2013;68:654-662.
20. Stroup DF, Berlin JA, Morton SC, Olkin I, Williamson GD, Rennie D, et al. Meta-analysis of observational studies in epidemiology: a proposal for reporting. Meta-analysis Of Observational Studies in Epidemiology (MOOSE) group. JAMA 2000;283:2008-2012.
21. Miller IM, Ellervik C, Yazdanyar S, Jemec GB. Meta-analysis of psoriasis, cardiovascular disease, and associated risk factors. J Am Acad Dermatol 2013;69:1014-1024.
22. Egger M, Davey Smith G, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. BMJ 1997;315:629-634.
23. Zhu KJ, He SM, Zhang C, Yang S, Zhang XJ. Relationship of the body mass index and childhood psoriasis in a Chinese Han population: a hospital-based study. J Dermatol 2012;39:181-183.
24. Paller AS, Mercy K, Kwasny MJ, Choon SE, Cordoro KM, Girolomoni G, et al. Association of pediatric psoriasis severity with excess and central adiposity: an international cross-sectional study. JAMA Dermatol 2013;149:166-176.
25. Mahé E, Beauchet A, Bodemer C, Phan A, Bursztejn AC, Boralevi F, et al. Psoriasis and obesity in French children: a case-control, multicentre study. Br J Dermatol 2015;172:1593-1600.
26. Tom WL, Playford MP, Admani S, Natarajan B, Joshi AA, Eichenfield LF, et al. Characterization of lipoprotein composition and function in pediatric psoriasis reveals a more atherogenic profile. J Invest Dermatol 2016;136:67-73.
27. Lee A, Smith SD, Hong E, Garnett S, Fischer G. Association between pediatric psoriasis and waist-to-height ratio in the absence of obesity: a multicenter Australian study. JAMA Dermatol 2016;152:1314-1319.
28. Choon SE, Ngim CF, Premaa S, Tey KW, Nalini MN. Clinico-epidemiological profile, including body mass index of Malaysian children with psoriasis. Med J Malaysia 2016;71:171-176.
29. Kwa L, Kwa MC, Silverberg JI. Cardiovascular comorbidities of pediatric psoriasis among hospitalized children in the United States. J Am Acad Dermatol 2017;77:1023-1029.
30. Ergun T, Seckin Gencosmanoglu D, Karakoc-Aydiner E, Salman A, Tekin B, Bulbul-Baskan E, et al. Prevalence of obesity in paediatric psoriasis and its impact on disease severity and progression. Australas J Dermatol 2017;58:e182-e187.
31. Hunjan MK, Maradit Kremers H, Lohse C, Tollefson M. Association between obesity and pediatric psoriasis. Pediatr Dermatol 2018;35:e304-e305.
32. Paller AS, Schenfeld J, Accortt NA, Kricorian G. A retrospective cohort study to evaluate the development of comorbidities, including psychiatric comorbidities, among a pediatric psoriasis population. Pediatr Dermatol 2019;36:290-297.

33. Caroppo F, Ventura L, Belloni Fortina A. High blood pressure in normal-weight children with psoriasis. Acta Derm Venereol 2019;99:329-330.
34. Cohen AD, Dreiher J, Shapiro Y, Vidavsky L, Vardy DA, Davidovici B, et al. Psoriasis and diabetes: a population-based cross-sectional study. J Eur Acad Dermatol Venereol 2008;22:585-589.
35. Goldminz AM, Buzney CD, Kim N, Au SC, Levine DE, Wang AC, et al. Prevalence of the metabolic syndrome in children with psoriatic disease. Pediatr Dermatol 2013;30:700-705.
36. Tollefson MM, Van Houten HK, Asante D, Yao X, Maradit Kremers H. Association of psoriasis with comorbidity development in children with psoriasis. JAMA Dermatol 2018;154:286-292.
37. de Ferranti SD, Gauvreau K, Ludwig DS, Neufeld EJ, Newburger JW, Rifai N. Prevalence of the metabolic syndrome in American adolescents: findings from the Third National Health and Nutrition Examination Survey. Circulation 2004;110:2494-2497.
38. Zimmet P, Alberti KG, Kaufman F, Tajima N, Silink M, Arslanian S, et al. The metabolic syndrome in children and adolescents - an IDF consensus report. Pediatr Diabetes 2007;8:299-306.
39. Ma C, Harskamp CT, Armstrong EJ, Armstrong AW. The association between psoriasis and dyslipidaemia: a systematic review. Br J Dermatol 2013;168:486-495.
40. Lønnberg AS, Skov L, Skytthe A, Kyvik KO, Pedersen OB, Thomsen SF. Association of psoriasis with the risk for type 2 diabetes mellitus and obesity. JAMA Dermatol 2016;152:761-767.
41. Gisondi P, Fostini AC, Fossà I, Girolomoni G, Targher G. Psoriasis and the metabolic syndrome. Clin Dermatol 2018;36:21-28.
42. Lu Y, Chen H, Nikamo P, Qi Low H, Helms C, Seielstad M, et al. Association of cardiovascular and metabolic disease genes with psoriasis. J Invest Dermatol 2013;133:836-839.
43. Boehncke WH, Boehncke S, Tobin AM, Kirby B. The 'psoriatic march': a concept of how severe psoriasis may drive cardiovascular comorbidity. Exp Dermatol 2011;20:303-307.
44. Armstrong EJ, Harskamp CT, Armstrong AW. Psoriasis and major adverse cardiovascular events: a systematic review and meta-analysis of observational studies. J Am Heart Assoc 2013;2:e000062.
45. Takeshita J, Grewal S, Langan SM, Mehta NN, Ogdie A, Van Voorhees AS, et al. Psoriasis and comorbid diseases: implications for management. J Am Acad Dermatol 2017;76:393-403.
46. Danielsen K, Wilsgaard T, Olsen AO, Furberg AS. Overweight and weight gain predict psoriasis development in a population-based cohort. Acta Derm Venereol 2017;97:332-339.
47. Naldi L, Addis A, Chimenti S, Giannetti A, Picardo M, Tomino C, et al. Impact of body mass index and obesity on clinical response to systemic treatment for psoriasis. Evidence from the Psocare project. Dermatology 2008;217:365-373.
48. Puig L. Obesity and psoriasis: body weight and body mass index influence the response to biological treatment. J Eur Acad Dermatol Venereol 2011;25:1007-1011.
49. Bronckers IM, Paller AS, van Geel MJ, van de Kerkhof PC, Seyger MM. Psoriasis in children and adolescents: diagnosis, management and comorbidities. Paediatr Drugs 2015;17:373-384.
50. Badaoui A, Tounian P, Mahé E. Psoriasis and metabolic and cardiovascular comorbidities in children: a systematic review. Arch Pediatr 2019;26:86-94.
51. Eichenfield LF, Paller AS, Tom WL, Sugarman J, Hebert AA, Friedlander SF, et al. Pediatric psoriasis: evolving perspectives. Pediatr Dermatol 2018;35:170-181.
52. Wild S, Roglic G, Green A, Sicree R, King H. Global prevalence of diabetes: estimates for the year 2000 and projections for 2030. Diabetes Care 2004;27:1047-1053.
53. Hansen ML, Gunn PW, Kaelber DC. Underdiagnosis of hypertension in children and adolescents. JAMA 2007;298:874-879.
54. Reilly JJ, Kelly J. Long-term impact of overweight and obesity in childhood and adolescence on morbidity and premature mortality in adulthood: systematic review. Int J Obes (Lond) 2011;35:891-898.
55. Falkner B. Hypertension in children and adolescents: epidemiology and natural history. Pediatr Nephrol 2010;25:1219-1224.
56. Pinhas-Hamiel O, Zeitler P. Acute and chronic complications of type 2 diabetes mellitus in children and adolescents. Lancet 2007;369:1823-1831.
57. Pappadis SL, Somers MJ. Hypertension in adolescents: a review of diagnosis and management. Curr Opin Pediatr 2003;15:370-378.
58. Wong J, Molyneaux L, Constantino M, Twigg SM, Yue DK. Timing is everything: age of onset influences long-term retinopathy risk in type 2 diabetes, independent of traditional risk factors. Diabetes Care 2008;31:1985-1990.
59. Donaghue KC, Chiarelli F, Trotta D, Allgrove J, Dahl-Jorgensen K. Microvascular and macrovascular complications associated with diabetes in children and adolescents. Pediatr Diabetes 2009;10 Suppl 12:195-203.
60. Schmidt MD, Magnussen CG, Rees E, Dwyer T, Venn AJ. Childhood fitness reduces the long-term cardiometabolic risks associated with childhood obesity. Int J Obes (Lond) 2016;40:1134-1140.
61. Cohen JB, Cohen DL. Cardiovascular and renal effects of weight reduction in obesity and the metabolic syndrome. Curr Hypertens Rep 2015;17:34.
62. Eder L, Joshi AA, Dey AK, Cook R, Siegel EL, Gladman DD, et al. Association of tumor necrosis factor inhibitor treatment with reduced indices of subclinical atherosclerosis in patients with psoriatic disease. Arthritis Rheumatol 2018;70:408-416.
63. Hjuler KF, Bøttcher M, Vestergaard C, Bøtker HE, Iversen L, Kragballe K. Association between changes in coronary artery disease progression and treatment with biologic agents for severe psoriasis. JAMA Dermatol 2016;152:1114-1121.
64. Elnabawi YA, Dey AK, Goyal A, Groenendyk JW, Chung JH, Belur AD, et al. Coronary artery plaque characteristics

and treatment with biologic therapy in severe psoriasis: results from a prospective observational study. Cardiovasc Res 2019;115:721-728.
65. Elnabawi YA, Oikonomou EK, Dey AK, Mancio J, Rodante JA, Aksentijevich M, et al. Association of biologic therapy with coronary inflammation in patients with psoriasis as assessed by perivascular fat attenuation index. JAMA Cardiol 2019;4:885-891.