

Quantitative analysis on the development of musculoskeletal adverse effects of corticosteroids using common data model

Sun Geu Chae¹, Sang-Heon Kim², Yoon-Kyoung Sung², Yeesuk Kim³

¹Department of Industrial Engineering, Hanyang University, Seoul, Korea

²Department of Internal Medicine, Hanyang University College of Medicine, Seoul, Korea

³Department of Orthopaedic Surgery, Hanyang University College of Medicine, Seoul, Korea

Background

- Corticosteroids are the most widely used and effective treatments for various inflammatory and autoimmune disorders due to strong anti-inflammatory effects.
- Despite their beneficial effects, long-term systemic (oral or parenteral) use of these agents is associated with well-known musculoskeletal adverse events (AEs) such as osteoporosis, bone fractures and osteonecrosis.
- Moreover, although the AE of corticosteroid usage is well known, the relationship between dosage and AE has not been determined thoroughly.



- The purpose of this study was to perform the quantitative analysis about the adverse events of the corticosteroid using common data model

Methods

- Data collected between 2001 and 2018 from OMOP Common Data Model of Hanyang University Seoul Hospital
- Patients aged between 25 and 64
- Inclusion: Systemic corticosteroids for the treatment of autoimmune diseases
- Exclusion: previous history of hip fracture and caisson disease - predisposing factor of index outcomes

- Outcomes of interest: osteoporosis, bone fracture, and osteonecrosis - musculoskeletal AEs of corticosteroids

Outcome	ICD-10 Code	ICD-9 Code	ICD-10 Code	ICD-9 Code
Osteoporosis	M85.00	730.00	M85.00	730.00
Fracture	S62.00	86.00	S62.00	86.00
Osteonecrosis	M86.00	730.00	M86.00	730.00

- Statistical analysis
 - Crude incidence rates of outcomes
 - Calculation of dose using Prednisolone Equivalent Dosage
 - Evaluation methods for dose related factor: Logistic regression model / Binary classification



- Using logistic regression modeling to determine the probability of outcomes in accordance with the cumulative dosage and daily average dosage of prednisolone equivalent, as well as the period of corticosteroid usage resulting in musculoskeletal AEs
- Optimal cutoff points for prediction of outcomes were chosen to maximize sensitivity and specificity

- R package "SteroidDoseStudy" : <https://github.com/estone96/SteroidDoseStudy.git>

Results

- 15,127 patients were included in this study.
- 1342 osteoporosis, 278 fracture, and 118 osteonecrosis patients
- The crude incidence rates : 8.9% (osteoporosis), 1.8% (fracture), 0.8% (osteonecrosis)
- The optimal cutoff point of cumulative dose: 1882mg (osteoporosis), 1425mg (fracture), 2312.5mg (osteonecrosis)
- The optimal cutoff point of daily dose: 4.7mg per day (osteoporosis), 5.4mg per day (fracture), 6.8mg per day (osteonecrosis)
- The optimal cutoff points of the corticosteroid period: 255 days (osteoporosis), 339 days (fracture), 439 days (osteonecrosis)



Figure a) Histogram of cumulative dose[mg] of PDS equivalent dose in osteoporosis cohort, b) Histogram of log scale cumulative dose, c) ROC curve d) Plot for determination of cutoff point of osteoporosis using maximal sum of sensitivity and specificity

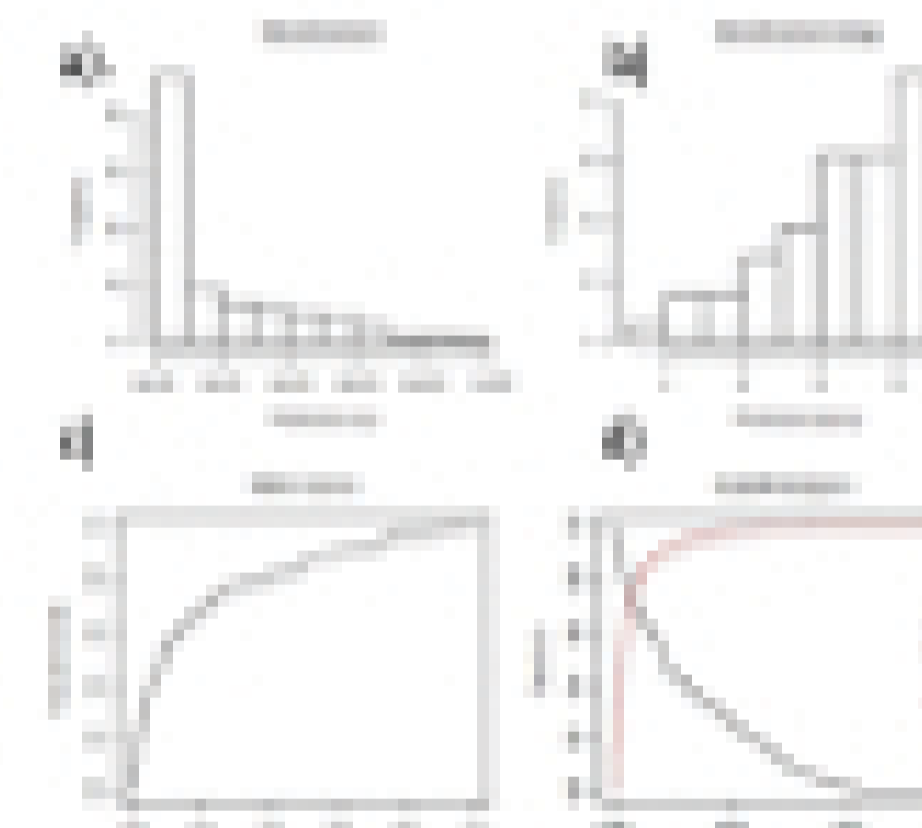


Figure a) Histogram of cumulative dose[mg] of PDS equivalent dose in fracture cohort, b) Histogram of log scale cumulative dose, c) ROC curve d) Plot for determination of cutoff point of fracture using maximal sum of sensitivity and specificity



Figure a) Histogram of cumulative dose[mg] of PDS equivalent dose in osteonecrosis cohort, b) Histogram of log scale cumulative dose, c) ROC curve d) Plot for determination of cutoff point of osteonecrosis using maximal sum of sensitivity and specificity

Conclusions

The incidence rate of muscular adverse effects were relatively low in our study, and a possible dose-response relationship was observed for bone related adverse effects. Therefore, our results support the need for developing new treatment strategies with a better safety profile than that of systemic corticosteroids.