A CLINICAL TOOL FOR AUTOMATED PREDICTION OF HIP AND MAJOR OSTEOARTROPLASTY FRACTURES USING ELECTRONIC MEDICAL RECORDS DATA: THE EPIC STUDY

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Background: With increasing availability of patient data in healthcare, there is an unprecedented opportunity for prediction tools that can be automatically implemented in electronic medical records system.

Methods: We aimed to develop and validate a fracture prediction tool that leverages patient data as routinely available in primary care computerized records.

Methods: We conducted a population-based cohort study. Data was extracted from all subjects registered in the SIDIAP database on 1/1/2012, with data for 1+ years, and aged 50 years or older on that date. SIDIAP contains primary care records linked to pharmacy dispensation for ~6 million people, equivalent to ~80% of the population of Catalonia. Participants were followed up until the earliest of death, transfer out/ migration, or end of 2017.

Two models were developed to predict hip fracture (main outcome) and major osteoporotic (hip, clinical vertebral, wrist/forearm, and proximal humerus) fracture risk over 5 years.

Potential predictors were pre-specified based on previous literature and combined in Cox models to derive prediction tools. Internal validation was performed using c-statistic for discrimination, and observed vs predicted plots for calibration. Multiple imputation with chained equations was used to minimize the impact of missing data on body mass index, smoking, and alcohol drinking. Bootstrapping methods were used to select key predictors to be combined in the final resulting models.

Results: A total of 1.76 million people (9.76 million person-years) were included, 50.7% women, of average age 65.4 years old. A 10.1% and 7.4% were lost to follow-up over 5 years due to mortality and migration respectively.

Fracture rates were 3.57/1000 person-years [95% CI] 3.53-3.60] for hip and 11.61 [11.54-11.68] for major fracture. Key predictors of increased fracture risk included age, female gender, history of falls or previous fractures, specific medication/s use (insulin, GnRH inhibitors, anticonvulsants, sedatives, SSRI, antipsychotics), and a history of diabetes mellitus (type 1 vs type 2), cerebrovascular disease, ischemic heart disease, COPD and anorexia nervosa. Variables associated with lower fracture risk included type 2 diabetes mellitus (type 2), hypertension, or end of 2017.

Conclusion: We have developed and validated a clinical prediction tool for 5-year hip and major osteoporotic fracture risk. The algorithm has excellent performance and can be installed in electronic primary care records systems for automated risk calculations at the population level. More research is needed on the transportability and external validity of this prediction tool.

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THE IMPACT OF ORAL GLUCOCORTICOIDS ON THE DEVELOPMENT OF CATARACTS AND GLAUCOMA IN INCIDENT RHEUMATOID ARTHRITIS PATIENTS

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Background: Cataracts and glaucoma are recognised glucocorticoid (GC) adverse effects. However, the impact of GC use, dose and timing on the development of cataracts and glaucoma has not been well quantified.

Objectives: 1. To determine the association between GC use and dose and the development of cataract and glaucoma in patients with incident RA, 2. To determine the lag effect of GC dose.

Methods: Data were used from the Clinical Practice Research Datalink (CPRD), a large UK primary care database derived from an electronic medical record (Jan 1992-Dec 2017). RA patients were identified using a validated algorithm and only incident patients were included. Parametric log-logistic survival models were used to assess the impact of GC use, dose (prednisolone daily dose equivalent) and lagged dose (at 1, 3, 6 months, 1 & 2 years). A square root transformation of dose was used for the cataract models. Smoking, gender and uveitis were included as covariates in the model and age was used as the timescale.

Results: There were 22607 patients with incident RA (median age 66, IQR 37-84, 68% female), of whom 241 had cataracts and 164 had glaucoma on or before baseline. Median duration of follow up was 8.7 years (IOR 1.8-19.8) and 39% were ever GC users during follow up. The incidence rate, per 1000 patient-years was 12.3 (95% CI 11.8, 12.9) for cataracts and 3.1 (95% CI 2.8, 3.4) for glaucoma, and increased with age. Uveitis was an important predictor for both cataracts and glaucoma, and cataracts were more frequent in females. GC use and GC dose were associated with both cataracts and glaucoma (Table 1). In the multivariable lagged dose analysis, GC dose at 1-year prior had the greatest effect size for cataracts (OR 1.26, 95% CI 1.12, 1.42), whereas GC dose at 3-months prior had the greatest effect size for glaucoma (OR 1.06, 95% 1.01, 1.11).

Conclusion: The quantification of the risk associated with GCs and the development of cataract and glaucoma is of clinical utility in daily practice. EULAR guidelines recommend patients are informed of the risks and benefits of GC treatment prior to commencement, however the risk of these potential adverse effects had not previously been quantified. This information will allow patients to make better-informed treatment choices in conjunction with their treating doctor.

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and all of them are associated with a high burden of comorbidities. Incidence of these diseases and of their comorbidities are unknown in Belgium.

Objectives: To determine incidences of disease and comorbidities in patient populations of RA, PSA and SPA in a General Practitioners (GP) setting.

Methods: Data were obtained from Intego over a 13-year time interval from 1999 to 2012. Intego is a Flemish GP-based morbidity registration network hosted at the Academic Center for General Practice of KU Leuven, covering 2% of the Flemish general population. Patients classified under the International Classification of Primary Care codes L88 (rheumatoid/seropositive arthritis) and L99 (musculoskeletal disease other) were selected for this study. Experienced rheumatologists verified if the keywords mapped to these codes corresponded to a diagnosis of RA/SPA/PSA. The entry date of these diagnoses in Intego was considered “baseline”.

Yearly disease incidence and comorbidity incidence over 3 years are presented. The following comorbidities with high impact on outcomes like disability, costs, hospitalization and death were considered: lung disease, cardiovascular disease including myocardial infarction, stroke or other heart condition, hypertension, fracture of the spine/hip/leg, depression, diabetes mellitus, digestive disease including ulcers and stomach disorders and malignancies [1].

Results: Over a 13-year period, 817, 258 and 190 patients were included with a diagnosis of RA, PSA or SPA, respectively. The average incidence of RA was 0.47, of PSA 0.15 and of PSA 0.11 per 1000 person years (Fig1) gives the yearly incidence per disease. The RA cohort had a mean(SD) age of 77.1(17.2) with 68% being women. The SPA cohort had a mean(SD) age of 40.6(15.1) with 50% being women. The PSA cohort had a mean(SD) age of 47(13.2) with 48% being women.

The comorbidity with the highest prevalence (23%) and incidence (29.6/1000 person years) in RA was hypertension. In the SPA cohort, digestive disease was most common at baseline (14%) and during follow-up (21.0/1000 person years), PSA patients presented most frequently with depression at baseline (18%) and during follow-up (9.8/1000 person years), RA patients presented with a higher number of incident cases of diabetes (17.7/1000 person years) compared to SPA or PSA patients. (See table 1)

Conclusion: The incidence of RA appears to remain stable while incidence of PSA - and to a lower extent SPA - seem to increase over a 13-year interval. A control cohort will be formed to improve comparability of comorbidity presence, yet from these preliminary results we can determine that an important subpopulation of patients with rheumatic diseases already presents with significant comorbidities at baseline, or during 3-year follow-up. This study highlights the growing issue of multimorbidity in patients with musculoskeletal diseases and the importance of a holistic approach to manage these patients.

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Background: Immunotherapy has revolutionized the treatment of cancer. The use of checkpoint inhibitors aimed at stimulating the immune system to mediate regression of established malignant tumors has shown a noticeable increase in the last decade. However, immunotherapy has been associated with side effects novel to cancer patients such as immune-related adverse events (IAEs) that can affect any organ or system, either during the course of immunotherapy or once the treatment was completed.

Objectives: To survey the occurrence and type of AAEs in 190 cancer patients treated with immunotherapy between 2011 and 2018.

Methods: We surveyed the occurrence of IAEs in cancer patients who received immunotherapy in the Oncology Service at the Virgen del Rocio University Hospital (Seville, Spain) between 2011-2018. The cases of cancer present in the patients analysed included: non-small cell lung cancer (NSCLC), small cell lung cancer (SCLC), melanoma, kidney cancer, bladder cancer and others. The check points inhibitors analysed included Iplilimumab (CTLA-4), Nivolumab (PD-1), Pembrolizumab (PD-1) and Atezolizumab (PD-L1). The nature of IAEs (rheumatic/non-rheumatic), the magnitude of complaint (mild/moderate/severe) and the outcome of patients depending on IAEs management was analysed. Finally, we used a multivariate analysis in search for patterns in IAE occurrence depending on cancer type, patient and treatment factors.

Results: A total of 190 patients were collected, 143 men and 47 women having NSCLC (51.1%), melanoma (25.3%), kidney cancer (6.8%), bladder cancer (5.3%), SCLC (2.1%) and others. They received immunotherapy with Atezolizumab (15.8%), Iplilimumab (4.7%), Nivolumab (61.1%) and Pembrolizumab (18.4%). Overall, 28 patients (14%) developed an AAE secondary to immunotherapy. Four of them involved rheumatic diseases (1 seronegative polyarthritis, 1 inflammatory myopathy and 2 rheumatic polymyalgia), whereas other non-rheumatic diseases were observed: 13 endocrine (12 thyroiditis and 1 DM type I debut with ketoacidosis), 5 pulmonary (pneumonitis), 3 dermatological (2 atopic dermatitis and 1 psoriasis), 2 digestive (colitis and autoimmune pancreatitis) and 1 neurological (hypophysitis). The drug that showed the highest occurrence of IAEs was Nivolumab (30%). In these patients, IAEs were associated with a median number of cycles of 7 (Q1 = 4, Q3 = 17.7, non-parametric data, Shapiro-Wilk test, p <0.0001). Mild adverse events occurred in 60% of patients

SA0594 ADVERSE AUTOIMMUNE EVENTS IN CANCER PATIENTS TREATED WITH IMMUNOTHERAPY. ANALYSIS OF CASES BETWEEN 2011 AND 2018

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with IAEs, for which immunotherapy was not suppressed. However, the medication was suppressed in the remaining 40% of the cases. Exceptionally, one patient underwent a severe IAE (pneumonitis) that resulted in death. In terms of the occurrence of IAEs, there was no difference between sexes (men 6.3%, women 6.4%). The rheumatic IAEs responded well to treatment with corticosteroids without further biological treatments or DMARDs.

Conclusion: Immunotherapy is changing the typology of side effects in cancer patients, including IAEs. The cases analysed showed a relatively small number of rheumatic events that were easily solved with corticosteroids (nor the immunotherapy treatment was suppressed or immunosuppressive treatment was necessary). The study highlights the benefits of involving multidisciplinary medical teams to manage oncology patients treated with immunotherapy towards the early detection and treatment of IAEs.

REFERENCES

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SAT0595

DIRECT COMPARISON OF CERTOLIZUMAB PEGOL, ABATACEPT AND BIOSIMILAR INFLIXIMAB IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED IN ROUTINE CARE. OBSERVATIONAL DATA FROM THE DANISH DANBIO REGISTRY ANALYZED LIKE A RANDOMIZED CLINICAL TRIAL

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Background: Nationwide Danish guidelines regarding RA patients (pts) initiating bDMARDs are issued approximately annually. For bio-naive pts on concomitant methotrexate (MTX) the recommended drugs (year, recommended compliance) were: certolizumab pegol (CTZ)/Abatacept (ABA)/biosimilar infliximab (CT-P13) 2013-2014, 80%; Abatacept (ABA)/biosimilar infliximab (CT-P13) 2015-2016, 50%. We hypothesized that the guidelines could be perceived as a surrogate randomization tool where calendar-time rather than patient-specific factors defined choice of bDMARD.

Methods: Observational cohort study analyzed like a randomized clinical trial (RCT, intention-to-treat). RA patients were identified in DANBIO. Compliance in each calendar period was defined as number of pts adherent to guideline/numbers of all bio-naive pts initiating bDMARD. Outcomes were DAS28-remission (at 6 and 12 months) and one-year retention rates, compared according to guidelines (confounder-adjusted multivariable logistic and Cox regression analyses).

Results: Compliance to guidelines was 70%/65%/59%, and 776 patients were included (CTZ/ABA/CT-P13: 336/215/225). Baseline characteristics were similar across drugs. CT-P13 remission-rates after 6 and 12 months were: 37%/34%/44% and 37%/33%/36%, respectively. Adjusted odd ratios for achieving CT-P13 remission were at 6 months: 0.96 (95% CI: 0.61, 1.5) for ABA and 1.38 (0.92-2.1) for CT-P13; 12 months: 0.74 (0.51, 1.2) and 0.96 (0.61, 1.5), CT reference drug (figure). The adjusted hazard ratios for withdrawal were 1.16 (95% CI: 0.84-1.60) for ABA and 0.83 for CT-P13 (0.59-1.17) (table).

Table. RA patients starting first bDMARD according to Danish national guidelines during the three calendar periods. Baseline characteristics and adjusted hazard ratios (HR) for withdrawal during the first year of treatment (Cox regression analyses).

<table>
<thead>
<tr>
<th></th>
<th>Certolizumab pegol</th>
<th>Abatacept</th>
<th>CT-P13 N=225</th>
</tr>
</thead>
<tbody>
<tr>
<td>N=336</td>
<td>1.0 (ref)</td>
<td>0.78 (0.45 to 1.36)</td>
<td>1.0 (ref)</td>
</tr>
<tr>
<td>Male</td>
<td>0.96 (0.61 to 1.60)</td>
<td>0.74 (0.45 to 1.17)</td>
<td>1.36</td>
</tr>
<tr>
<td>Female</td>
<td>0.96 (0.61 to 1.60)</td>
<td>0.74 (0.45 to 1.17)</td>
<td>1.10</td>
</tr>
<tr>
<td>Age, years</td>
<td>57 (48-65)</td>
<td>57 (48-65)</td>
<td>59 (50-66)</td>
</tr>
<tr>
<td>Female</td>
<td>77%</td>
<td>72%</td>
<td>72%</td>
</tr>
<tr>
<td>Hazard ratio for withdrawing treatment 90-365 days</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adjusted for age and gender</td>
<td>1.0 (ref)</td>
<td>1.0 (ref)</td>
<td>1.0 (ref)</td>
</tr>
<tr>
<td>Male</td>
<td>1.15 (0.85 to 1.56)</td>
<td>1.15 (0.85 to 1.56)</td>
<td>1.15 (0.85 to 1.56)</td>
</tr>
<tr>
<td>Female</td>
<td>1.16 (0.84 to 1.60)</td>
<td>1.16 (0.84 to 1.60)</td>
<td>1.17 (0.83 to 1.60)</td>
</tr>
</tbody>
</table>

Variables are median (IQR) unless otherwise mentioned. *age, gender, DAS28, HAQ, smoking, CCI Abbreviations: CCI: Charlson Comorbidity Index; CI: confidence intervals, DAS28: Disease Activity Score of 28 joints, HAQ: Health assessment questionnaire.

Conclusion: Compliance to guidelines was high. Direct comparison showed that remission and retention rates were highest for CT-P13, intermediate for certolizumab and lowest for abatacept. Results should, however, be interpreted with caution due to wide CIs and risk of residual confounding.

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