Доклади на Българската академия на науките
Comptes rendus de l'Académie bulgare des Sciences
Tome 77, No 9, 2024

MEDICINE
Clinical medicine

COULD ASA AND CHARLSON COMORBIDITY INDEX SCORES HELP THE CURRENT COMORBIDITIES STRATIFICATION IN NON-SURGICAL KNEE OSTEOARTHRITIS MULTIMODAL PAIN MANAGEMENT?

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Received on November 18, 2021
Presented by D. Damianov, Member of BAS, on November 30, 2021

Abstract

Non-surgical management of knee osteoarthritis emphasizes on multimodal approach according to patients subphenotypes (with or without comorbidities). Surgical treatment outcomes data suggest the role of ASA and Charlson Comorbidity Index (CCI) scores in the field. There are no comparative data on ASA and CCI stratification in non-surgical knee osteoarthritis pain management, which is the aim of our study.

Eighty ASA 1–3 in-hospital patients, aged ≥ 36, treated for symptomatic chronic knee osteoarthritis with implemented intra-articular Betamethasone (7 mg/ml) or Hyaluronic acid (30 mg/2 ml), followed by as needed Dexketoprofen 50 mg i.v. or Paracetamol 1.0 g i.v., along with recommended 2 weeks (10 working days) exercise-based physiotherapy programme were examined retrospectively. Data regarding demographics, comorbidities, ASA low-risk(1–2)/high-risk(3), CCI low-risk(0–1/0–2)/high-risk($\geq$ 2/ $\geq$ 3) scoring subgroups, effusions, WBC, ESR, vital signs, clinical laboratory parameters, adverse events, and analgesic consumptions were collected as well. We tested the effect of different ASA and CCI scores on analgesic consumption (primary outcomes), and the effect of implemented risk-adjusted multimodal analgesia on subsequent participation or non-participation in the physiotherapy programme (secondary outcomes). Among all outcomes variables, ASA and CCI stratification confirmed only the higher age and ESR determinants in both the high-risk ASA 3

https://doi.org/10.7546/CRABS.2024.09.13

and high-risk CCI ≥ 2 subgroups, as well as more Hyaluronic acid applications in the elderly. The participants in the physiotherapy programme were mainly low-risk patients who received significantly more intra-articular Hyaluronic acid than Betamethasone. The ASA and CCI scores could help current (yes/no comorbidities) decision-making by implementing risk-adjusted pain management, emphasizing on severity rather than the type of comorbid conditions in non-surgical knee osteoarthritis population.

Key words: ASA/CCI risk-adjustment, intra-articular Betamethasone/ Hyaluronic acid, knee osteoarthritis

Introduction. Osteoarthritis (OA) is the most common form of arthritis, affecting millions of people worldwide. OA is characterized by pathology involving the whole joint, including cartilage degradation, bone remodelling, osteophyte formation, and synovial inflammation, leading to pain, stiffness, swelling and loss of normal joint function [1]. Knee OA accounts for four fifths of the burden of OA worldwide and increases with obesity and age. The global prevalence of knee OA was 16% in individuals added 15 and over. At continent-level, the prevalence was higher in Asia (19.2%) than in Europe (13.4%) and North America (15.8%) [2].

Recent guidelines for non-surgical management of knee OA emphasize on multimodal analgesic treatment according to patients subphenotypes (with or without comorbidities) [3]. Data from surgical treatment of knee OA support more precisely the role of comorbidities on adverse outcomes in patients with different American Society of Anesthesiologists (ASA) and Charlson Comorbidity Index (CCI) scores [4]. There are no comparative data on ASA and CCI stratification in non-surgical knee osteoarthritis pain management, which is the aim of our study.

Materials and methods. Eighty ASA 1–3 in-hospital patients, aged ≥ 36, treated for symptomatic chronic knee osteoarthritis (the American Rheumatism Association criteria [5]) with implemented intra-articular (IA) Betamethasone (7 mg/ml) or Hyaluronic acid (HA)(30 mg/2 ml), followed by as needed Dexketoprofen 50 mg i.v. or Paracetamol 1.0 g i.v., along with recommended 2 weeks (10 working days excluding the weekends) exercise-based physiotherapy programme were examined retrospectively. Under local anesthesia with Lidocaine, the intra-articular Betamethasone or Hyaluronic acid were injected at superolateral patellar site in the "dry" knee (without effusion or after evacuation of the effusion). The physiotherapy programme comprised 10 minutes flexibility (m.biceps femoris, m.semimembranosus, m.semitendinosus and m.gastrocnemius) and strengthening (m.vastus lateralis, m.vastus medialis, and m.vastus intermedius) supervised exercises. Patients who attended the programme were instructed to continue their exercises after discharge as often as possible, as long as possible, and as intensively as possible. The needs for repetitive intra-articular injections and/or for exercise-based physiotherapy were checked at 6-month intervals or during rehospitalisation(s) (as needed). Data regarding demographics, comorbidities, ASA

low-risk(1–2)/high-risk(3), CCI low-risk(0–1/0–2)/high-risk($\geq 2/ \geq 3$) subgroups scoring, effusions, WBC, ESR, vital signs, clinical laboratory parameters, adverse events, and analgesic consumptions were collected as well. We tested the effect of different ASA and CCI scores on analgesic consumption (primary outcomes), and the effect of implemented risk-adjusted multimodal analgesia on subsequent participation or non-participation in the physiotherapy programme (secondary outcomes). All statistical analyses were performed at $\alpha = 0.05$.

Results. The within-group comparisons revealed significantly more high-risk ASA patients according to age (10 years older), gender (more female patients), higher WBC, ESR and blood sugar levels, whereas CCI patients confirmed these findings only for age (significantly in score ≥ 2, and as a tendency in score ≥ 3 subgroups) and ESR levels (significantly in score ≥ 2 subgroup) (Table 1).

From all tested baseline confounding variables, the whole-group IA analgesic consumption was influenced only by age (62.62 ± 10.35 years in favour of HA, 47/80 (59%), compared to Betamethasone 33/80, (41%) ($p = 0.023$). After implementing the ASA and CCI scoring, the subgroup-analysis revealed significantly more low-risk (ASA 1–2, CCI 0–1) and high-risk (CCI ≥ 2) patients treated with HA as well (Fig. 1). There was no difference in systemic analgesic consumption (Fig. 2).

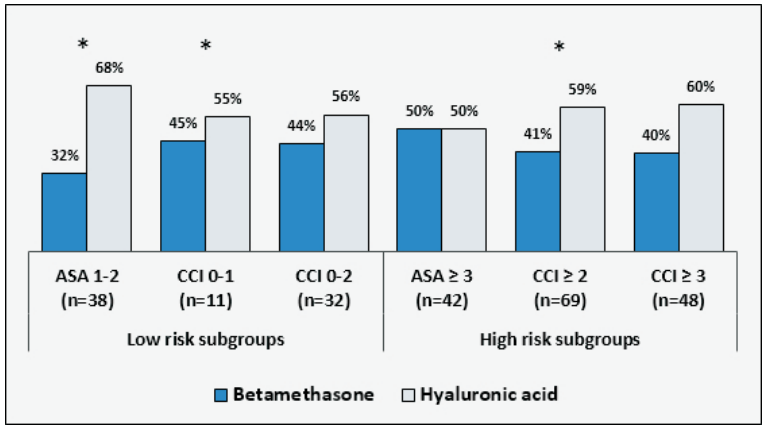

Fig. 1. IA analgesic consumption (%) according to ASA and CCI risk subgroups scoring ($^*p < 0.05$)

Of 22/80 (27.5%) rehospitalized patients (within 2 years of their first in-hospital admission), twice as many were treated with IA HA (15/22, 68%) as compared to those treated with IA Betamethasone (7/22, 32%) ($p = 0.02$), at the expense of a two-fold increase of low-risk (ASA 1–2) subgroup patients as well ($p < 0.0001$). Only 3/80 (4%) patients were prescribed (as needed) oral opioids along with IA Betamethasone and systemic analgesics (during their first-time in-hospital admission).

The participants in the physiotherapy programme were mainly low-risk pa-

Table 1

Demographic and baseline data after standard ASA and restrictive CCI risk subgroups scoring (mean±SD, unless otherwise specified)

	Low risk (ASA 1–2; n=38)	High risk (ASA $\geq$ 3; n=42)	p	Low risk (CCI 0–1; n = 11)	High risk (CCI $\geq$ 2; n=69)	p
Age (years)	60.2 ± 9.6	70.1 ± 9.3	0.001	56.5 ± 11.2	66.8 ± 9.9	0.002
Gender (Male/Female)	3/35	13/29	0.010	1/10	15/54	0.330
HR (beat/min)	70.68 ± 8.98	70.55 ± 8.31	0.944	72.45 ± 9.81	70.32 ± 8.41	0.684
Systolic AP (mm Hg)	130.37 ± 9.85	130.24 ± 14.90	0.964	133.91 ± 9.90	129.72 ± 13.03	0.272
Diastolic AP (mm Hg)	80.26 ± 7.07	79.60 ± 9.10	0.717	78.64 ± 5.52	80.12 ± 8.51	0.377
Mean AP (mm Hg)	96.96 ± 7.29	6.48 ± 10.00	0.805	97.06 ± 6.12	96.65 ± 9.15	0.966
Glucose (fasting)(mmol/l)	5.87 ± 0.71	7.63 ± 1.65	0.003	8.73 ± 5.80	16.58 ± 13.46	0.042
WBS ($\times 10^9$/l)	6.46 ± 1.78	7.63 ± 1.65	0.003	6.90 ± 2.27	7.10 ± 1.73	0.442
ESR (mm/h)	12.03 ± 12.77	18.64 ± 12.44	0.022	8.73 ± 5.80	16.58 ± 13.46	0.042
Effusions (Yes/No)	11/27	13/29	0.845	4/7	20/49	0.620
Rehospitalization(s)(Yes/No)	13/25	9/33	0.201	4/7	18/51	0.352

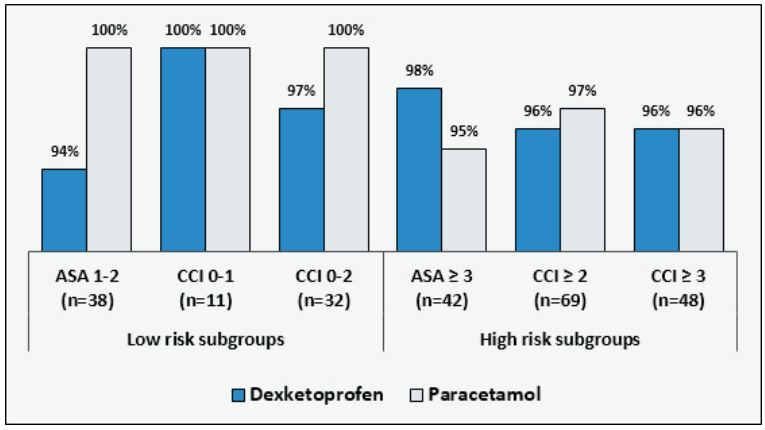

Fig. 2. Systemic analgesic consumption (%) according to ASA and CCI risk subgroups scoring

tients who received significantly more IA HA. Those who did not attend the programme were with significantly more abnormally accelerated ESR, an indication for the presence of inflammation and predominantly high-risk patients (Table 2).

The within-group comparison revealed that low-risk physiotherapy participants received twice as much HA as Betamethasone (IA Betamethasone (ASA 1–2) 9/41 (22%) vs. IA Hyaluronic acid (ASA 1–2) 18/41 (44%), $p = 0.035$). Among the patients who refused the physiotherapy programme, those with high-risk score received four times more Betamethasone than low-risk non-participants (IA Betamethasone (ASA 1–2) 4/39 (10%) vs. IA Betamethasone (ASA $\geq$ 3) 15/39 (38%), $p = 0.004$).

Discussion. Although there is strong evidence on the effect of comorbidities, IA injections, ASA and CCI on adverse surgical outcomes after total knee arthroplasty (TKA) [4], there is limited research of their overall impact on non-surgical OA treatment [6]. The latest 2019 Osteoarthritis Research Society International (OARSI) guidelines for the non-surgical management of knee OA, for the first time provide guidance for OA patients with particular four comorbidities (gastrointestinal, cardiovascular, frailty and widespread pain/depression) [3]. They strongly recommended a core exercise-based physiotherapy treatment for all patients (regardless of the comorbidities in question), and conditionally recommended the use of IA corticosteroids (CS) and IA HA in individuals with knee OA in all groups, as well. Our data on non-surgical knee OA multimodal pain management are in line with the proposed OARSI vision of a comorbidity-adjusted approach. However, we refined and expanded the applicability of this approach, focusing on the severity of the disease (ASA scoring) and on the comorbidity burden (CCI scoring), rather than on the particular comorbidities in our patients. To our knowledge there are no other findings on this subject matter, and our study fills the gap on this issue.

Table 2

Inflammatory data and intra-articular analgesic consumption according to ASA and CCI risk subgroups scoring in patients who participated or refused the physiotherapy programme

	With physiotherapy $n = 41$	Without physiotherapy $n = 39$	p
Abnormally Increased WBC	4 (10%)	5 (13%)	0.675
Abnormally Accelerated ESR	3 (7%)	9 (23%)	0.045
Effusions	14 (34%)	10 (26%)	0.438
Low-risk ASA (1–2)	27 (66%)	11 (28%)	0.0007
Low-risk CCI (0–1)	9 (22%)	2 (5%)	0.028
High-risk ASA (≥ 3)	14 (34%)	28 (72%)	0.0007
High-risk CCI (≥ 2)	32 (78%)	36 (92%)	0.083
Betamethasone (ASA 1–2)	9 (22%)	4 (10%)	0.147
Betamethasone (CCI 0–1)	5 (12%)	0 (0%)	0.159
Hyaluronic acid (ASA 1–2)	18 (44%)	8 (21%)	0.029
Hyaluronic acid (CCI 0–1)	4 (10%)	2 (5%)	0.401
Betamethasone (ASA ≥ 3)	8 (19%)	15 (38%)	0.061
Betamethasone (CCI ≥ 2)	12 (29%)	17 (44%)	0.165
Hyaluronic acid (ASA ≥ 3)	6 (15%)	13 (33%)	0.060
Hyaluronic acid (CCI ≥ 2)	20 (49%)	19 (48%)	0.929

In light of the COVID-19 pandemic and the measures to limit the aerosol spread of the disease, our approach suggests significant advantages for more severely ill knee OA patients. In patients who had to have TKA and who had to delay it because of the lockdown, there was a significant increase in pain, worsening of physical function, and a decrease in physical activity. The European League Against Rheumatism (EULAR) suggests IA CS and IA HA, along with exercises for those OA patients in a home care setting in order to alleviate pain, improve function and quality of life [7]. The IA HA injections in high-risk (CCI $>$ 2) patients improve survival without TKA by an average of 7.1 months and their application is even more relevant in the conditions of COVID-19 pandemic [8]. The majority of our high-risk patients sooner or later are potentially surgical candidates. Hence from surgical perspective, our patient-centred ASA/CCI adjusted optimization of their knee OA pain and function along with the optimization of cardiorespiratory status before surgery by means of IA Betamethasone or IA HA followed by exercise-based physiotherapy does matter [9].

In terms of IA analgesics usage, our data are relatively comparable with the data from the OA Initiative [10]. The observed shift in our practice from IA CS towards IA HA could be explained by growing evidence in favour of HA [11] (on the background of the ongoing debate on its modest (+ placebo) effectiveness [12,13]), as well as with the findings of greater cartilage volume loss and no significance in knee pain relief after repetitive IA CS treatment compared to IA saline [14]. Yet, IA CS have their role in flares of knee OA, especially with effusions. Recent evidence suggests that after 3 months IA CS have no greater effect on pain than placebo and may be inferior to physical therapy active comparator at 1 year [15], whereas IA HA may have beneficial effect on pain at and beyond 12 weeks of treatment along with a more favourable long-term safety profile than repeated IA CS [3]. Our whole-group IA analgesic consumption was influenced only by age in favour of more IA HA in the elderly ($p = 0.023$). This is in line with the available evidence that IA HA is a good option for older patients receiving poly-pharmacy due to the HA low potential for adverse effects and drug-drug interactions [16]. In addition, the majority of our patients who participated in physiotherapy programme received more IA HA than IA CS. Thus our clinical practice confirms the role of IA HA for combination therapy with exercise-based physiotherapy suggested by others [16]. On the contrary, those who refused physiotherapy received more IA CS than IA HA. Most of them had abnormally accelerated ESR which could explain increased CS usage in the presence of inflammation, along with probably lower muscle strength for the same reason (cut-off point for muscle weakness at ESR $\geq$ 16 mm/h, reported by others [17]).

As to our systemic analgesic usage (Fig. 2), our data differ from those of the Amsterdam OA cohort [18], probably because of the inevitable bias with the "enrichment" of our in-hospital cohort with more severely ill non-surgical patients who suffer from stronger and more widespread OA pain. Such an oversampling

is a common practice in conducting knee OA research (e.g. the inclusion of only patients listed for joint replacement, or with effusions only, or in our case with indications for IA injections only), when the authors aim for homogeneity of the sample at the expense of generalizability of their results [19]. This limits the translation of our research into out-hospital clinical practice as well.

Conclusions. The ASA and CCI stratification reconfirmed the limitations in the real-life prescribed multimodal pain management. Nevertheless, they could help current (yes/no comorbidities) decision-making in the field by emphasizing on severity rather than the type of comorbid conditions in non-surgical knee osteoarthritis population.

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