

Effects of Anticholinergic Burden on Autonomic Function, Pain, and Physical Impairment in Patients with Knee Osteoarthritis

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INTRODUCTION: Patients with late-stage osteoarthritis (OA) often present with comorbidities and concurrent medical conditions. The use of multiple medications can result in anticholinergic effects, which may suppress the pain- and inflammation-modulating effects of parasympathetic activity. In this study, we investigated whether and how the anticholinergic burden, as measured by the Anticholinergic Cognitive Burden (ACB) score, affects heart rate variability (HRV), pain, and physical impairment in OA patients.

METHODS: The ACB score was assessed in OA patients (n = 148; 80 females, 68 males) and healthy controls (n = 40; 24 females, 16 males) before and one year after total knee arthroplasty (TKA) using an online calculator (<https://www.acbcalc.com/>). Heart rate (HR), pulse, and HRV parameters—sympathetic activity: low-frequency (LF) power; parasympathetic activity: high-frequency (HF) power, pNN50, RMSSD, SDRR—were analyzed using short-term ECG recordings. Additionally, pain, stiffness, and physical impairment were evaluated using the WOMAC score. The effects of the ACB score on cardiovascular parameters, WOMAC outcomes, and their interactions were examined using mixed linear regression models, with age, sex, and BMI included as confounders.

RESULTS SECTION: 17.5% of healthy controls and 56.5% of OA patients were taking anticholinergic medications, particularly analgesics (0% vs. 51%), antihypertensives (27% vs. 63%), diuretics (7% vs. 31%), anticoagulants (2% vs. 26%), antidiabetics (5% vs. 20%), statins (5% vs. 24%), antidepressants (7% vs. 12%), and/or NSAIDs (2.5% vs. 1.3%). OA patients exhibited a significantly higher ACB score compared with controls ($ACB_{\text{healthy}}=0.17\pm 0.38$, $ACB_{\text{OA}}=0.84\pm 1.22$, $p=0.007$). One year after TKA, the ACB_{OA} score did not significantly change (post- $ACB_{\text{OA}} = 0.77 \pm 1.12$). In men, a higher ACB was associated with a significantly increased pulse rate (+18.12 bpm per logACB, 95% CI 1.95–34.28, $p=0.028$). Moreover, the association between the log-transformed ACB_{OA} score and pulse significantly differed by gender (interaction estimate: -18.38 bpm per log(ACB) unit, 95% CI: -36.64 to -0.12, $p=0.049$): in female patients, each one-unit increase in log(ACB) was associated with a non-significant increase in pulse (+5.48 bpm, $p=0.318$). In patients with low ACB_{OA} score (mean-1SD) before surgery, RMSSD increased after when compared to pre-TKA values (estimate +4.01, CI 0.14–2.64, $p=0.030$), which is not observed in patients with high ACB_{OA} scores (mean+1SD) at baseline. The pre-TKA ACB_{OA} score was negatively associated with WOMAC impairment of physical function, with each one-unit increase in the log ACB_{OA} score corresponding to a 103.82-point decrease (95% CI -203.02 to -4.62, $p=0.040$). However, in individuals with higher heart rate (HR), this relationship was attenuated and even reversed, as indicated by a significant interaction (estimate: +1.30 per log(ACB) score unit per one-unit increase in HR, 95% CI 0.01-2.59, $p=0.048$). Similar effects were observed for the WOMAC total score, where a higher ACB_{OA} score was associated with a 101.72-point reduction (95% CI: -191.97 to -11.47, $p=0.027$), and this association was also reversed in patients with higher HR (interaction estimate: +1.25 per log(ACB) score unit per one-unit increase in HR, 95% CI: 0.08-2.42, $p=0.036$). Age and BMI did not exhibit any significant influence.

DISCUSSION: Our findings demonstrate that patients with late-stage knee osteoarthritis exhibit a higher anticholinergic burden compared to non-OA controls. Among patients undergoing TKA, elevated preoperative anticholinergic exposure was associated with alterations in autonomic function. Specifically, higher ACB scores correlated with changes in heart rate, reflecting increased sympathetic activity, with patterns differing by sex. Additionally, patients with lower baseline ACB showed a significant post-TKA increase in RMSSD, indicative of improved autonomic regulation, whereas this recovery was absent in those with higher baseline ACB.

SIGNIFICANCE/CLINICAL RELEVANCE: These results suggest that minimizing anticholinergic exposure prior to surgery may beneficially affect autonomic function and improve clinical outcomes in OA patients.