

and *in vitro/ex vivo* tests. Together with the sometimes highly elevated titres and persistence of positive tests for up to 2 yr, we think these findings likely reflect an IgE rebound phenomenon because of intercurrent use of pholcodine-containing antitussives, which is known to be associated with elevated total IgE.⁹

Evidence is emerging that occupancy of MRGPRX2 receptors could constitute a novel endotype of IDHRs, including anaphylaxis from NMBAs. Here, we show that a generic mechanistic reclassification may be incorrect. In the majority of patients, the diagnosis of an IgE-mediated reaction to rocuronium is established by a combination of skin tests and *in vitro/ex vivo* tests. To the best of our knowledge, this is the first attempt to explore clinical and biological features in IgE-dependent and likely MRGPRX2-dependent rocuronium anaphylaxis. If our classification is correct, it seems that clinical details, acute tryptase, and delta tryptase are indistinguishable. In contrast, skin mast cells that strongly express MRGPRX2¹¹ appear to be less sensitive in the MRGPRX2-dependent group. In the absence of a reference test to document MRGPRX2-dependent anaphylaxis, and because of the longer interval between index reaction and testing, it cannot be excluded that some patients with negative *in vitro/ex vivo* tests (the possible MRGPRX2 group) have in fact experienced an IgE-dependent reaction. Thus, we firmly discourage any re-administration of NMBAs in skin-test-positive patients, irrespective of the results of *in vitro/ex vivo* tests.

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Declarations of interest

The authors declare that they have no conflicts of interest.

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Factors affecting need for manipulation after total knee arthroplasty: a retrospective case–control cohort study

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Editor—Manipulation under anaesthesia (MUA) after total knee arthroplasty (TKA) is an undesirable postoperative outcome. Studies have failed to find a single causative factor leading to the

need for postoperative MUA.^{1,2} We sought to determine whether perioperative analgesia via peripheral nerve block was associated with the incidence of MUA after TKA.

Table 1 Results from multivariable logistic regression model predicting knee manipulation. CDHP, consumer-driven health plan; CI, confidence interval; EPO, exclusive provider organisation; HDHP, high-deductible health plan; HMO, health maintenance organisation; IQR, inter-quartile range; OME, oral morphine equivalent; OR, odds ratio; POS, point of service; PPO, preferred provider organisation; PT, physical therapy.

Variable	Knee manipulation	
	OR (95% CI)	P-value
Peripheral nerve block	1.03 (0.97–1.09)	0.304
Age	0.96 (0.96–0.97)	<0.001
Sex		
Female	Reference	
Male	0.80 (0.76–0.85)	<0.001
Charlson–Deyo index		
0	Reference	
1	1.06 (0.99–1.13)	0.079
2	0.86 (0.76–0.98)	0.024
3	0.85 (0.73–0.99)	0.037
Obesity	0.78 (0.72–0.84)	<0.001
Sleep apnoea	0.90 (0.80–1.01)	0.075
Depression	0.70 (0.64–0.77)	<0.001
Opioid naïve	1.12 (1.06–1.18)	<0.001
Region		
Northeast	Reference	
North Central	1.19 (1.09–1.30)	<0.001
South	1.04 (0.96–1.14)	0.326
West	1.31 (1.19–1.45)	<0.001
Unknown	1.13 (0.83–1.53)	0.438
Median household income (\$US)		
<45 000	Reference	
45 000–60 000	1.05 (0.95–1.17)	0.354
>60 000	1.02 (0.88–1.17)	0.807
Unknown	1.02 (0.92–1.14)	0.693
Insurance plan type		
Comprehensive	Reference	
EPO	0.84 (0.63–1.13)	0.259
HMO	0.99 (0.86–1.14)	0.885
POS	0.80 (0.68–0.94)	0.005
PPO	0.86 (0.76–0.97)	0.013
POS with capitation	1.44 (1.05–1.98)	0.022
CDHP or HDHP	0.82 (0.71–0.94)	0.003
Unknown	1.13 (0.88–1.46)	0.346
Year of procedure		
2013	Reference	
2014	1.00 (0.92–1.08)	0.950
2015	0.92 (0.85–1.00)	0.049
2016	0.88 (0.80–0.96)	0.003
2017	1.05 (0.96–1.14)	0.313
Type of procedure		
Unilateral	Reference	
Bilateral	1.10 (1.00–1.21)	0.043
Length of stay	1.02 (1.01–1.03)	0.001
Discharge status		
Home	Reference	
Home health service	1.07 (1.01–1.13)	0.024
Other or unknown	1.13 (1.01–1.28)	0.039
Transfer to other facility	1.09 (0.99–1.19)	0.089
Total OME within 1 yr after surgery	1.00 (1.00–1.00)	<0.001
PT sessions within 3 months after surgery	1.01 (1.01–1.01)	<0.001

The Hospital for Special Surgery (New York, NY, USA) Institutional Review (IRB #2017-0169) approved this study. Patients undergoing TKA from January 1, 2013 to December 31, 2017 were identified from the Truven Health MarketScan database (Truven Health Analytics, Inc., IBM, Armonk, NY, USA). We identified 205 966 TKA procedures using the International Classification of Diseases, Ninth Revision procedure code 81.54 or Tenth Revision procedure codes 0SRCOXX and OSRDOXX. Patients who were not continuously enrolled between procedures or for at least 1 yr before or after their initial surgery ($n=95\ 934$), patients <18 yr old ($n=45$), and duplicate records or patients who had multiple TKA surgeries during the study period were excluded ($n=12\ 795$). The primary outcome of interest was if a patient received MUA (Current Procedural Terminology code 27570) within 1 yr after TKA. The primary exposure of interest was the receipt of a peripheral nerve block (Current Procedural Terminology codes 64445–64450). Additional covariates included patient age, sex, Charlson–Deyo comorbidity index,³ obesity, sleep apnoea, depression, preoperative history of opioid use, region of the USA, median household income (in \$US), insurance plan, year of surgery, surgery type (bilateral or unilateral), length of stay (days), discharge status, total oral morphine equivalents within the first year after surgery, and number of physical therapy sessions billed within the first 3 months after surgery.

Descriptive analyses were stratified by receipt of MUA within 1 yr after TKA. Categorical variables were reported as frequencies (%) and compared using χ^2 tests, whilst continuous variables were reported as median (interquartile range [IQR]) using Wilcoxon rank-sum tests. A multivariable logistic regression model was run for the binary outcome of MUA within 1 yr. The main effect, peripheral nerve block, was included in the models in addition to other covariates of interest. Results with a $P<0.05$ were considered statistically significant. All analyses were conducted using SAS, version 9.4 (SAS Institute, Inc., Cary, NC, USA).

We identified 97 192 patients who underwent TKA procedures during the study period. Within the first year after surgery, 6036 (6.2%) received MUA. The median (IQR) time to knee manipulation was 62 (48–87) days. Amongst those receiving and not receiving MUA, 2965 (49.1%) and 43 631 (47.9%) received peripheral nerve block, respectively ($P=0.058$). Differences in covariates between groups can be seen in [Supplementary Table 1](#). After adjustment, peripheral nerve block remained a non-significant predictor for MUA after TKA (odds ratio: 1.03; 95% confidence interval: 0.97–1.09; $P=0.304$) ([Table 1](#)).

Postoperative supervised physiotherapy remains the first line of defence against development of arthrofibrosis.⁴ A

recent nationwide study in Sweden found an incidence of 1.7% for MUA, with cases more likely amongst healthy, younger, female patients.⁵ A recent review of the literature concluded that a comprehensive valid risk model for the need for MUA is lacking.⁶ A Cochrane review of randomised trials showed that peripheral nerve block for knee surgery is associated with improved postoperative pain control up to 72 h after surgery.⁷ In this retrospective case–control cohort study of 97 192 patients, we did not find an association between peripheral nerve block and need for MUA within 1 yr after TKA. Further studies are necessary to explore whether postoperative pain trajectories and regional anaesthetic approaches can influence the need for MUA after TKA.

Declarations of interest

The authors declare that they have no conflict of interest.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.bja.2020.10.007>.

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