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Frailty and long-term postoperative disability trajectories: a prospective multicentre cohort study

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Abstract

Background: Frailty is associated with early postoperative outcomes. How frailty influences long-term postoperative recovery is poorly described. Our objective was to evaluate the association of frailty with postoperative disability trajectories in the year after surgery.

Methods: Prespecified 1-yr follow-up of a prospective multicentre cohort study. Patients ≥65 yr were assessed for frailty before major elective noncardiac surgery (Clinical Frailty Scale [CFS] and Fried Phenotype [FP]). The primary outcome was patient-reported disability score (using the WHO Disability Assessment Schedule 2.0) at baseline, 30, 90, and 365 days after surgery. Repeated measures linear regression estimated the association of preoperative frailty with changes in disability scores over time, adjusted for procedure. Group-based trajectory modelling was used to identify subgroup trajectories of people with frailty.

Results: One-year follow-up was complete for 687/702 (97.9%) participants. Frailty was associated with a significant difference in disability trajectory ($P<0.0001$). Compared with baseline, people with frailty experienced a decrease in disability score at 365 days (CFS frailty: −7.3 points, 95% confidence interval [CI] −10.2 to −4.5); (FP frailty: −5.4 points, 95% CI −8.5 to −2.3); people without frailty had no significant change in their disability score from baseline (no CFS frailty: +0.8 points, 95% CI −1.7 to 3.2; no FP frailty: +1.1 points, 95% CI −3.5 to 1.3). More than one-third of people with frailty experienced an early increase in disability before achieving a net decrease in disability.

Conclusions: Decision-making and care planning should integrate the possible trade-offs between early adverse outcomes with longer-term benefit when frailty is present in older surgical patients.

Keywords: disability; epidemiology; frailty; postoperative outcome; recovery; surgery

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Editor's key points

- Patient frailty has become widely recognised as an important risk factor in surgery.
- This study found that frailty markedly affects long-term recovery and health after surgery.
- Interestingly, disability scores in those with frailty improved significantly more over time.
- Frailty status should not be used as a barrier to providing care.

Frailty is a syndrome related to the accumulation of age- and disease-related deficits that results in vulnerability to adverse health outcomes.[1,2] In the setting of major surgery, frailty is strongly and consistently associated with poor postoperative outcomes, including an approximately two-fold increase in the likelihood of serious morbidity and mortality, and a greater than five-fold increase in the odds of non-home discharge.[3–9] Additionally, frailty predicts adverse patient-reported outcomes, including a ≥two-fold increase in the odds of developing a new or significantly worsened disability within 90 days of surgery[5] and reduced health-related quality of life.[6]

However, most studies of frailty and adverse postoperative outcomes have only evaluated in-hospital and early postoperative outcomes (i.e. within 30–90 days). Although some studies do address 1-yr mortality rates,[8–10] few studies provide data on long-term patient-reported or functional outcomes; fewer still address long-term outcomes using repeated measures of patient-reported outcomes to understand recovery trajectories. In fact, to our knowledge, only one study (single-centre, limited to aortic valve surgery) has evaluated postoperative recovery trajectories.[11] Accordingly, international experts have recently highlighted the need for longitudinal data on trajectories experienced by older people with frailty as a key knowledge gap.[12]

To address the lack of long-term trajectory data regarding the association of frailty with patient-reported outcomes, we conducted a planned 1-year follow-up of patients enrolled in a multicentre cohort study of older patients having major elective noncardiac surgery. Our specific objectives were three-fold. First, we aimed to compare disability scores over time between individuals with and without frailty (defined using two validated frailty instruments, the Clinical Frailty Scale [CFS][1] and the Fried Phenotype [FP][13]). Next, we aimed to describe the association between frailty and the occurrence of death or new disability 1 yr after surgery. Finally, we undertook an exploratory analysis using group-based trajectory modelling to evaluate disability trajectories in the year after surgery in people with frailty.

Methods

Design and study setting

This was a multicentre prospective cohort study conducted across three separate hospitals in Ottawa, Ontario, Canada. A protocol has been previously published,[14] and primary early outcomes (death or new disability 90 days after surgery) have been disseminated.[5] A specific protocol for 1-yr analysis was not published. The current study was a planned analysis of 365-day follow-up data.[5,14] The three hospitals involved included a community hospital, a regional tertiary cancer referral centre, and a tertiary referral centre for spine, vascular, neurosurgery, and trauma. Recruitment occurred between September 1, 2015 and June 30, 2017. The last 365-day follow-up took place in July 2018. Ethical approval was obtained from the Ottawa Health Sciences Network Research Ethics Board and the Montfort Research Institute (Protocol Approval #20150342-01H and DM-31-08- 15, respectively). Results are reported according to appropriate guidelines.[15]

Study population, inclusion, and exclusion criteria

We enrolled all individuals who provided written informed consent if they were ≥65 yr of age on the day of their elective noncardiac surgery with expected length of stay of ≥2 days. Participants also had to have working knowledge of English or French and be reachable by telephone after hospital discharge. Individuals with mild to moderate cognitive dysfunction who were able to answer outcome scales were also eligible for enrolment; if cognitive impairment precluded informed consent by the individual, a decision-making proxy could provide consent.

Exposures

The presence of frailty before surgery was documented independently using two validated and well-studied frailty instruments (the CFS[1] and FP).[2] The CFS is a 9-point global rating scale, with a score assigned based on assessment of mobility, energy levels, physical activity, and function; scores ≥4 identified the presence of frailty. The FP is based on the measurement of gait speed, grip strength, activity levels, history of weight loss, and falls; individuals with ≥3 deficits present were categorised as having frailty. All frailty assessments were conducted by a trained Clinical Research Assistant (CRA; training description supplementary Table S1) or the primary study physician (DIM). All frailty assessments conducted by CRAs were audited by the primary study physician, although physician review led to no changes in assigned frailty scores (see Supplementary Table S1).

Outcomes

The primary outcome was the patient-reported disability score based on the WHO Disability Assessment Schedule 12-item (WHODAS), version 2.0,[16] which is validated in a variety of health conditions, including surgery.[17] Participants reported their disability score at baseline, 30, 90, and 365 days after surgery. The baseline assessment was performed in-person, as were any assessments performed for patients who remained in-hospital after surgery at an assessment point. Otherwise, assessments were reported by telephone to a trained research assistant who was blinded to frailty status. Each question was answered using a 0–4-point scale, with questions addressing issues across six domains of disability (cognition, mobility, self-care, getting along with others, life activities, participation in the community; two questions per domain). This produced a disability score ranging from 0 to 48, which was then expressed as a percentage of the maximum score on a 100-point scale. A score of 0 represents no disability, while a score of 100 represents total disability.[16] Normative data suggest an 8-point change in score to be clinically significant; findings reported after the conclusion of the study suggest a 5-point change may be significant in surgical patients.[18] Validation studies support a cut-off of 25 points to represent clinically significant disability.[19] Individuals who were no longer alive at follow-up were assigned a score of 100.

Secondary outcomes were death or new disability 365 days after surgery, a binary outcome defined using standard criteria as present if: a) a participant died, b) an individual had an increase in disability score (relative to baseline) of 8 or more points at follow-up.[17]

Covariates

Baseline demographic, comorbid, cognitive, and psycho-social characteristics were collected as outlined in detail in the study protocol.[14] Procedural characteristics were also collected.

Analysis

Descriptive statistics were calculated for individuals with and without frailty and compared between groups using absolute standardised differences. We considered absolute standardised differences exceeding 10 to indicate a substantive difference between groups.[20] We also described the average severity in each WHODAS domain at each time point by frailty status. All analyses were performed using SAS v 9.4 (SAS Institute, Cary, NC, USA). The level of significance for statistical testing was set at 5%.

The primary analysis compared repeated measures of the disability score between people with and without frailty from baseline over the 365 days after surgery (i.e. days 0, 30, 90, 365). To do this, the repeated disability score measures were analysed using linear mixed models using a restricted maximum likelihood approach. The unadjusted analysis included terms for frailty, categorical time, and frailty-by-time interaction. As the type of surgery can influence postoperative disability status and trajectory, our primary adjusted model was specified with an additional term for surgery type (as a categorical variable with orthopaedic [reference], intra-abdominal, vascular, thoracic, and neurosurgery categories). In our primary approach, we considered frailty-related conditions such as comorbidity, cognitive dysfunction, and falls history to be contributory to frailty; these were not included in the model to prevent over-adjustment bias. In peer-review it was requested that the primary analysis be repeated with adjustment for additional confounders (multimorbidity [≥2 Elixhauser comorbidities], sex, cognitive dysfunction, depression, and smoking), which was done as a sensitivity analysis. Least squares mean differences were calculated for each frailty-by-time interaction; adjustment for multiple comparisons were made using the Tukey-Kramer method.[21] To account for correlation in repeated measures over time, an unstructured covariance pattern was selected (which minimised the Akaike Information Criterion).

We also completed *post hoc* sensitivity analyses. Recognising that our specified primary analysis using disability scores as a continuous normal variable may have been impacted by non-adherence to the assumptions of linear regression, we performed the same analysis using a log transformed dependent variable. We also performed an analysis of possible effect modification by adding a multiplicative interaction term between frailty and surgery type. To examine whether trajectories may have differed based on the degree of frailty present, we performed an analysis where frailty status was defined as a three-level categorical variable (CFS 0–3 [reference], 4, ≥5; FP 0–1 [reference], 2, ≥3).

The association of frailty with death or new disability 365 days after surgery was analysed using unadjusted and adjusted (for surgery type, as in our primary analysis) Poisson regression with robust standard errors to generate risk ratios.[22]

As an exploratory analysis, we also performed group-based trajectory modelling to identify whether distinct subgroups of patients who followed similar disability trajectories over the first postoperative year were present among people with frailty. Disability scores were modelled using a censored normal distribution, and we considered models with three, four, and five possible trajectory groups. Separate models were fit for individuals identified with frailty using the CFS and FP. We identified the best fitting model for each frailty instrument (based on the lowest Akaike Information Criterion) and confirmed that the model had clinical validity through presentation to the multidisciplinary authorship group.[23,24] Model fits were confirmed through calculation of predicted group membership by actual group assignment (values >0.7 suggest good fit).[23,25]

Sample size

This was a planned 1-yr follow-up study of a cohort that was initially powered to detect a difference in relative true and false positive rates predicting 90-day death or new disability between the CFS and the FP. All participants with available outcome data were included in this analysis.

Missing data

As the method of restricted maximum likelihood analysis of repeated measures allows estimation of effect sizes even when missing values exist at some timepoints and our overall proportion of missing values was small, our analysis was based on all available data without imputation.

Results

Follow-up data were complete for 687 of the 702 participants who consented and underwent an eligible surgery (97.9% with complete follow-up; Fig. 1). Baseline characteristics are provided in Table 1, grouped by frailty status (291 [42.4%] had frailty per the CFS; 252 [36.7%] per the FP). The group with frailty included more people with orthopaedic and fewer with abdominal surgery than the group without frailty and were slightly older with higher rates of multimorbidity and depression. The most common procedures within each surgery type are provided in Supplementary Table S2.

Association of frailty with disability scores over time

Results for analyses using the CFS are presented here. Because results using the FP were similar, but the CFS is faster and easier to use for perioperative clinicians,[5] FP-specific findings are reported in Supplementary Table S3.

Baseline disability scores differed significantly between individuals with and without frailty using the CFS ($P<0.0001$). People without frailty had an average disability score of 13.3 (standard deviation 22.9) at baseline, while those with frailty had an average disability score of 26.9 (standard deviation 24.6).

The results from the repeated measures linear regression analysis are presented in Figure 2. With and without adjusting for surgery type, there were statistically significant differences between the groups at baseline and over time (each $P<0.0001$).

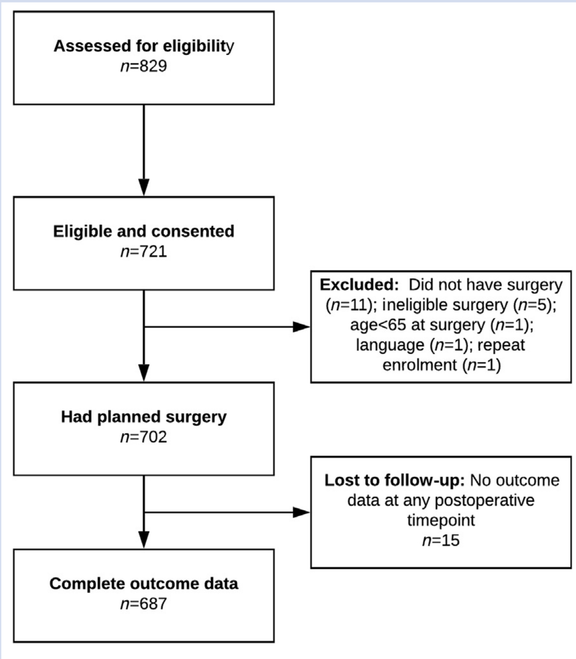

Fig 1. Cohort creation, reasons for exclusion and follow-up.

Table 1 Baseline cohort characteristics.

	Frailty	No frailty	ASD
	n=252	*n*=435	
Age, yr (mean, [SD])	74 [7]	73 [6]	15
Male sex (*n*, %)	106 [42.1]	247 [56.8]	30
Multimorbidity (*n*, %)	167 [66.3]	249 [57.2]	19
BMI, kg m^{-2} (mean, [SD])	32 [22]	30 [11]	11
Type of surgery (*n*, %) Orthopaedic	143 [56.8]	209 [48.1]	17
Abdominal	36 [14.3]	102 [23.5]	24
Thoracic	25 [9.9]	43 [9.9]	0
Neuro	15 [6.0]	19 [4.4]	7
Vascular	33 [13.1]	62 [14.3]	3
Cognitive impairment (*n*, %)	123 [48.8]	124 [14.5]	79
History of falls (*n*, %)	107 [42.5]	99 [22.7]	43
Depression (*n*, %)	34 [14.5]	18 [4.1]	36
Smoker (*n*, %)	80 [31.2]	158 [36.3]	11

ASD, absolute standardised difference; SD, standard deviation.

In contrast to those without frailty at baseline, disability scores in those with frailty improved significantly more over time; the least squares mean difference demonstrated an 7.3-point (95% confidence interval [CI] −10.2 to −4.5) *decrease* in disability score between baseline and 365 days after surgery for people with frailty, compared with a 0.8-point (95% CI −1.7 to 3.2) *increase* in disability score for people without frailty using the CFS. The between-group difference in mean disability score change from baseline to 1 yr after surgery was significant (8.1-point decrease for people with frailty compared with without, *P*<0.0001). Results of the log-transformed and categorical frailty analyses were consistent

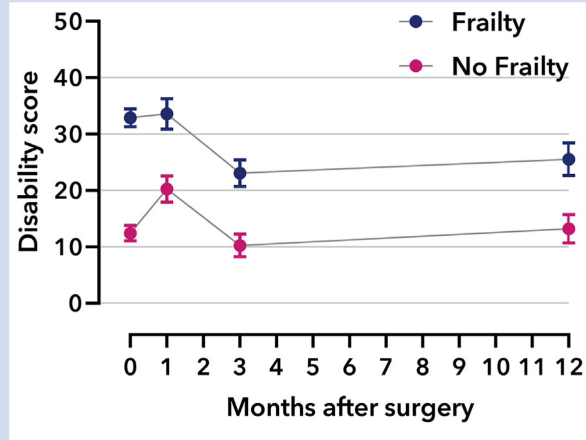

Fig 2. Least squares mean disability scores at baseline, 1, 3, and 12 months after surgery for people with and without frailty. Least squares mean values are adjusted for surgery type.

and are presented in Supplementary Table S4. There was no evidence of effect modification by surgery type (*P*-value for interaction=0.62). A heat map of average WHODAS domain severity over time by frailty status is provided in Figure 3. The *post hoc* analysis with additional covariate adjustment demonstrated minimal change in the between-group difference at 1 yr (8.0-point decrease for people with frailty compared with without, *P*<0.0001).

Association of death or new disability 1 yr after surgery with frailty

At 1 year follow-up, 51 (17.6%) people with frailty had died or were experiencing a new or clinically significantly higher disability (13 dead, 38 disabled), compared with 74 (18.6%) (19 dead, 65 disabled) people without frailty (unadjusted risk ratio 0.94, 95% CI 0.68−1.30; *P*=0.71). After adjustment for surgery type, having frailty on the CFS before surgery was not significantly associated with increased risk of death or disability (adjusted risk ratio 1.16, 95% CI 0.84−1.48; *P*=0.33).

Exploratory group-based trajectory models

A four-group trajectory model was found to be most consistent with our data and was considered clinically appropriate (Fig. 4). Model fit statistics are provided in Supplementary Table S5 and demonstrated excellent fit (probability of assigned membership >0.9 for all groups). Among people with frailty based on the CFS, two groups (which represented 95% of participants) had a decrease in disability from baseline to 1 yr (steady decrease trajectory and decrease after acute increase trajectory), however, more than one-third of patients experienced an early increase in disability after surgery before regaining a positive recovery trajectory. Two small groups experienced an increase in disability (steady increase trajectory and increase after initial recovery trajectory).

Discussion

We found that people with frailty had significantly greater disability at baseline than people without frailty, but that they

Fig 3. WHO Disability Assessment Score domain severity over time, by frailty status (according to the Clinical Frailty Scale). This figure plots the severity in each domain and item using a heat map (see Legend, inset).

experienced a significantly greater *improvement* in their disability scores over the year after elective noncardiac surgery. However, the presence of frailty was associated with a challenging recovery trajectory after surgery for one-third of patients. These novel, patient-reported outcome data provide important insights for older people considering surgery and the clinicians who care for them.

Two to three hundred million surgical procedures occur globally each year,[26] mostly in older adults.[27,28] Approximately 30%–40% of older surgical patients live with frailty.[5,10] Given the well-established association between frailty and risk of early morbidity and mortality, an understandable degree of caution exists when discussing surgery with older people living with frailty, or in decision-making on the part of older people with frailty, their families, and clinicians.[29,30] To date, however, the literature lacks studies that provide longitudinal patient-reported outcome data after common noncardiac surgeries. These data are of particular importance to older people with frailty because this population typically places a high value on functional outcomes and because the indication for surgery may be a primary contributor to the presence of frailty.[31] In other words, longitudinal patient-reported outcome data that capture key elements of day to day function are needed to help inform whether the risks of early adverse outcomes may be balanced by the potential of longer-term benefit from surgery.

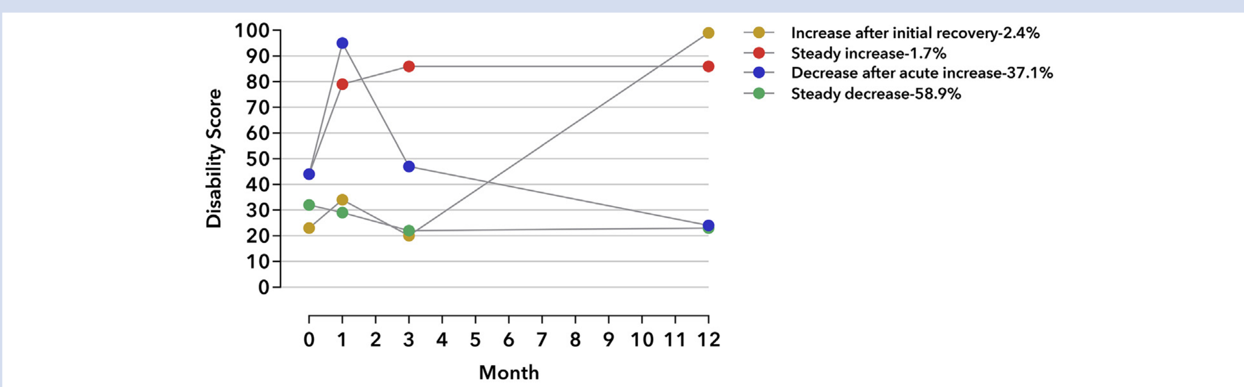

Fig 4. Group-based disability trajectories over the first postoperative year for people with frailty based on the Clinical Frailty Scale. Each trajectory group is based on the best fitting group-based trajectory model based on the lowest Akaike Information Criterion value; the percent of the cohort with frailty assigned to each group is provided in the trajectory description.

The current study begins to address the knowledge gap related to postoperative recovery trajectories in older people with and without frailty. As expected, people with frailty had higher disability scores before surgery (frailty and disability are distinct, but related concepts[32]) and, as shown in our previous work, had a 2.5-fold increase in their odds of experiencing a new or clinically significantly worsened disability within 3 months of their operation.[5] However, by 12 months after surgery, people with frailty (regardless of the instrument used to measure it) had experienced a larger decrease in disability, on average, than people without frailty. Importantly, for those whose frailty was identified using the CFS, the decrease in disability may be consistent with a clinically important improvement (eight points,[19] and as low as five points in surgical patients[18]). Additionally, there was no evidence that this effect differed significantly by the type of surgery. In contrast, older people without frailty did not experience a significant change in disability from baseline to 1 yr after surgery. This suggests that among older people with frailty who are undergoing noncardiac surgery, if the early perioperative period can be safely navigated, there may be meaningful benefit to gain from undergoing intermediate to high risk elective surgery. These findings also support statements from international frailty experts that frailty status should not be used as a barrier to providing care.[12,33]

The finding that older surgical patients with frailty may stand to benefit from their procedure to a greater extent than those without frailty across a variety of noncardiac surgeries stands in contrast to a large body of literature demonstrating increased risk of early adverse events for people with frailty[5–7,34–36] and requires consideration. First, people with frailty had higher levels of baseline disability than those without frailty; this may provide greater opportunity to improve over time. Second, when exploring distinct disability trajectories, we found that more than one-third of patients who eventually experienced a decrease in disability had a substantial increase in disability in the early postoperative period. This likely reflects the impact of acute surgical stress, the related four-fold increase in the odds of postoperative complications associated with frailty,[37] and loss of lower limb function that occurs with immobility in a catabolic postoperative state. However, our findings do suggest that many people with mild to moderate frailty (e.g. CFS 4–5) may have adequate resiliency to tolerate the stress of surgery, and potentially negotiate early adverse events, allowing them to experience a net decrease in disability 1 yr after surgery, although it should be stated that even with this decrease overall disability levels continue to be higher in people with frailty.

It must also be recognised, however, that small groups of people with frailty did experience a progressive increase in disability or die in the year after surgery. This suggests that future research to develop predictive models identifying such individuals before surgery is needed to differentiate those with frailty who are likely to have a positive postoperative disability trajectory *vs* those who are more likely to die or suffer a longstanding increase in disability. Identification of those likely to experience intermediate increases in disability could also help with care planning and health system optimisation strategies. Although our study was not designed or adequately powered to develop such models, these tools could inform the consent process and application of shared decision-making before surgery.

Strengths and limitations

As a prospective cohort study, we were able to obtain validated exposure and outcome measures by trained and blinded assessors, helping to reduce the risk of misclassification bias. Using data from three separate hospitals provides greater likelihood of generalisability than a single centre, however, all centres were in the same jurisdiction, therefore external verification should be pursued. Although the CFS and FP are two widely used instruments, we did not test the association of other frailty instruments (e.g. Edmonton Frail Scale, Frailty Index) with outcome; different underlying constructs between frailty instruments could lead to differing disability trajectories given the multiple domains captured by the WHODAS scale. All participants were selected to undergo surgery; therefore, our findings cannot be translated to individuals who may not be considered appropriate candidates for elective surgery. Furthermore, our data cannot be inferred as causal; randomisation would be required to test the causal association between surgery and significant decreases in disability in older people with frailty after surgery. We did not have data on need for nursing home or homecare supports at 1 year, therefore, the impact of disability on the health system was not measurable. Finally, our rates of death or new disability at follow-up were lower than anticipated based on early follow-up data, which could have left our study underpowered for the death or new disability outcome and precludes us from performing mortality-specific analyses.

Conclusions

In a multicentre prospective cohort study, we found that older people with frailty before elective noncardiac surgery were more likely to experience a significant decrease in disability in the first postoperative year than people without frailty. Surgical decision-making and informed consent with older surgical patients should include frailty assessment and discussion of higher short-term risks in the context of potential long-term benefits. Future research is needed to develop accurate tools to predict whether older surgical patients with frailty are likely to experience a decreasing or increasing postoperative disability trajectory, which should support care planning and shared decision-making.

Authors' contributions

Contributed to conception, design, data acquisition, interpretation and revised and approved the final manuscript: all authors
Contributed to analysis, drafted the final manuscript: DIM, AJF, CVW
Guarantor: DIM

Declarations of interest

PEB reports personal fees from Corin, personal fees from MicroPort, personal fees from Zimmer Biomet, personal fees from Medacta, personal fees from MatOrtho, grants from Zimmer Biomet, outside the submitted work. LTL reports grants and personal fees from Sanofi, personal fees from Ferring, outside the submitted work. The remaining authors declare that they have no conflicts of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.bja.2020.07.003.

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