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RESEARCH PAPER

The impact of frailty on short-term mortality following primary total hip and knee arthroplasty due to osteoarthritis

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Abstract

Background: We determined the association between frailty and short-term mortality following total hip and knee arthroplasty (THA/TKA) for osteoarthritis and also the impact of THA/TKA on short-term mortality compared with a control population.
Methods: Frailty was assessed using a frailty index (categorised: fit, mild, moderate, severe frailty). The association between frailty and short-term mortality following THA/TKA was assessed using Cox regression. Mortality following THA/TKA was also compared with a control population with osteoarthritis but no previous THA/TKA, matched on year of birth, sex and quintile of index of multiple deprivation.
Results: A total of 103,563 cases who had a THA, 125,367 who had a TKA and matched controls contributed. Among those who had surgery, mortality increased with increasing frailty; adjusted hazard ratio (HR) (95% CI) at 30 days in severely frail versus fit: following THA, 2.85 (1.84, 4.39) and following TKA, 2.14 (1.29, 3.53). The predicted probability of 30-day mortality following THA/TKA varied by age, sex and frailty: following THA, from 0.05% among fit women aged 60–64 years to 6.55% among men with severe frailty aged ≥90 years. All-cause 30-day mortality was increased in fit cases following THA and TKA, respectively, versus fit controls (adjusted HR (95% CI), 1.60 (1.15, 2.21) and 2.98 (1.81, 4.89)), though not among cases with mild, moderate or severe frailty versus controls in the same frailty category.
Conclusion: Short-term mortality increased with increasing frailty following THA/TKA. Comparison of mortality among cases and controls may be affected by a 'healthy surgery' selection effect.

Keywords: total hip arthroplasty, total knee arthroplasty, frailty, mortality, epidemiology, older people

Key Points

- Short-term mortality following total hip arthroplasty (THA) and total knee arthroplasty (TKA) increased with increasing frailty.
- The predicted 30-day mortality following THA and TKA varied by age, sex and frailty status; from 0.05 to 6.55% following THA.
- Compared with non-surgical controls with osteoarthritis (OA), short-term mortality following THA and TKA was influenced by level of frailty.
- Comparison of mortality among cases and controls may be biased due to a 'healthy surgery' effect.

Background

Among patients with osteoarthritis (OA), joint replacement surgery, including total hip arthroplasty (THA) and total knee arthroplasty (TKA), may be indicated in those who remain symptomatic despite conservative therapy. Both THA and TKA are associated with a short-term peak in mortality, which subsides in the 90-day period following surgery [1, 2]. A number of factors have been linked with increased mortality post-THA and -TKA, including age and also frailty [3–9].

Previous studies have indicated that mortality up to 90 days following THA and TKA increases with increasing frailty, independent of age [3–9]. However, frailty is associated also with increased mortality in the general population [10]. Therefore, it is not clear whether the impact of frailty on short-term mortality following hip and knee arthroplasty is different from the impact of frailty on mortality among individuals who do not have surgery. No previous studies have looked at the association between frailty and short-term mortality following THA and TKA among people with OA, which has been associated with an increased risk of mortality [11], compared with an age-, sex- and deprivation-matched control population who had OA but had not had joint surgery. Such data are important and may potentially help to inform shared decision-making between patients and healthcare professionals about whether to proceed with THA or TKA.

The aims of this study were, using large-linked primary and secondary care clinical databases from the UK, to determine the impact of frailty on the risk of 30-, 60- and 90-day mortality following THA and TKA, including predicted probability of short-term mortality by age, gender and frailty. Second, we determined the risk of short-term mortality among people who had a THA/TKA, compared with controls who had OA but no previous THA/TKA. We also looked at cause-specific mortality following THA/TKA and also among controls.

Methods

Data sources

We used a primary care clinical database from the UK; the Clinical Practice Research Datalink (CPRD) to carry out a retrospective cohort study [12, 13]. The CPRD was linked to secondary care medical records, the Hospital Episode Statistics (HES) [14] and also the Office for National Statistics (ONS) mortality database, using robust methods of data linkage [15]. The protocol for this work was approved by the Independent Scientific Advisory Committee for CPRD research (protocol number 20_119). CPRD has ethics approval from the Health Research Authority to support research using anonymised patient data.

Assessment of frailty

Frailty was assessed using the electronic Frailty Index (eFI) [16]. The eFI comprises 36 age-related deficits identified by coded data in primary care electronic medical records and was developed using a standard procedure [17] (Supplementary Table 1, Supplementary data are available in *Age and Ageing* online). In order to apply the eFI in practices using the SNOMED coding system, we mapped the original eFI Read code lists to SNOMED codes using mapping tables from the National Health Service Data Migration Programme [18].

The eFI is calculated as the total number of the eFI deficits present in an individual, divided by 36. Based on previously published thresholds, we categorised the eFI as fit ($eFI \leq 0.12$), mild frailty ($0.12 < eFI \leq 0.24$), moderate frailty ($0.24 < eFI \leq 0.36$) and severe frailty ($eFI > 0.36$) [16]. The eFI has been validated in multiple databases and criterion validity has been demonstrated by comparing the eFI to other frailty instruments, including the phenotype model of frailty and the Clinical Frailty Scale [16, 19, 20].

Identification of THA and TKA

We identified individuals who had a primary THA or TKA from 2 January 1998 to 31 March 2019 based on OPCS codes recorded in secondary care (HES) records, using code lists from the National Joint Registry [21]. We included people who were 60 years or older at the time of their THA or TKA, since the prevalence of frailty is relatively low at younger ages. We excluded people who had a THA or TKA with a primary indication for surgery relating to fractures, osteonecrosis, rheumatoid arthritis and malignant neoplasm of bone. In addition, we excluded cases where the coded primary indication for THA/TKA was used in <0.05% of cases.

Identification of hip and knee OA

We identified individuals with hip or knee OA based on diagnostic codes recorded in primary care electronic medical records (see Supplementary Table 2, Supplementary data are available in *Age and Ageing* online).

Statistical analysis

We matched individuals who had a THA or TKA (cases), respectively, to individuals who had a diagnostic code for hip or knee OA in their primary care record at the time of the arthroplasty of the case but had not had a THA or TKA recorded in the HES data prior to the date of THA or TKA of the matched case (controls). Matching was done on year of birth, sex and quintile of index of multiple deprivation (IMD). Each control was matched to one and only one case. We determined the eFI at the date of THA/TKA for cases and the date of THA/TKA of the matched case for controls.

We used Kaplan–Meir estimates to calculate 30-, 60- and 90-day mortality among cases. We plotted the hazard function for mortality among cases for the first 90 days following surgery, applying smoothing using changes in the Nelson-Aalen cumulative hazard estimate with band half-width 7 days.

Table 1. Participant characteristics

	Hip cohort		Knee cohort	
	Cases (THA), *n* = 103,563	Controls (hip OA), *n* = 103,563	Cases (TKA), *n* = 125,367	Controls (knee OA), *N* = 125,367
	Mean (SD)			
Age	72.6 (7.5)	72.6 (7.5)	72.3 (7.2)	72.3 (7.2)
	n (%)			
Female	63,405 (61.2)	63,405 (61.2)	71,169 (56.8)	71,169 (56.8)
Quintile of IMD				
1 (least deprived)	27,436 (26.5)	27,436 (26.5)	30,568 (24.4)	30,568 (24.4)
2	25,162 (24.3)	25,162 (24.3)	29,450 (23.5)	29,450 (23.5)
3	22,317 (21.6)	22,317 (21.6)	27,042 (21.6)	27,042 (21.6)
4	16,834 (16.3)	16,834 (16.3)	21,467 (17.1)	21,467 (17.1)
5 (most deprived)	11,759 (11.4)	11,759 (11.4)	16,747 (13.4)	16,747 (13.4)
Frailty category				
Fit	42,427 (41.0)	34,103 (32.9)	42,339 (33.8)	39,251 (31.3)
Mild frailty	42,181 (40.7)	42,055 (40.6)	55,845 (44.6)	52,822 (42.1)
Moderate frailty	15,269 (14.7)	20,158 (19.5)	22,056 (17.6)	24,875 (19.8)
Severe frailty	3,686 (3.6)	7,247 (7.0)	5,127 (4.1)	8,419 (6.7)

We determined the association between eFI category (referent category: 'fit') and 30-, 60- and 90-day mortality following THA/TKA using Cox regression, adjusted for sex, 5-year age bands, quintile of IMD and year of surgery. Results were presented as hazard ratios (HR) and 95% CI. The index date were the date of the THA/TKA. Participants contributed person-time from the index date to the date of death, the date the individual's primary care practice stopped contributing data to the CPRD, or after 90 days, whichever came first.

We estimated the predicted probability of 30-day mortality following hip and knee arthroplasty for men and women by 5-year age band and frailty category. We did this using a multivariable logistic regression model with year of surgery, frailty category, age band, sex and quintile of IMD included as covariates and calculated predicted probabilities using the 'margins' command in Stata. Covariates were set to their median values. We assessed the performance of the logistic model in predicting 30-day mortality by calculating the area under the receiver operating characteristic (ROC) curve.

We looked then at the association between case/control status and 30-, 60- and 90-day mortality, using Cox regression models, adjusted for age category, sex, quintile of IMD and eFI category. The index date for controls were the date of the THA/TKA of the matched case. Controls were censored if they had a THA or TKA during the follow-up period. To determine the influence of frailty status on mortality, we looked at the interaction between case/control status and frailty category. In the Cox regression models, clustering of matched pairs was taken into account and robust variance estimation was used to calculate the 95% CIs.

We performed sensitivity analyses when looking at the association between case/control status and mortality in order to mitigate possible residual imbalance in frailty between cases and controls within the same frailty strata. First, we adjusted for the eFI score, as a continuous variable. Second, we adjusted for each of the individual 36 deficits of the eFI.

We looked at the primary cause of death (by ICD code) in cases and controls. Because of the substantially fewer deaths due to neoplasms among the cases than controls, we looked also at the association between case/control status and 30-, 60- and 90-day mortality due to causes of death other than neoplasms, with deaths due to neoplasms modelled as a competing risks.

All primary care practices included in our analyses consented to data linkage to secondary care, ONS mortality IMD databases. Determination of the eFI, mortality, occurrence of THA and TKA and all covariates was possible for all study participants, with no missing data.

Analyses were carried out using Stata/MP v13.1.

Results

Participants

In total, 133,439 THAs and 139,211 TKAs were identified. After exclusions, 108,941 eligible THAs and 125,439 eligible TKAs remained. Suitable controls were found for 103,563 (95%) eligible THA cases and 125,367 (>99.9%) eligible TKA cases and these cases and controls were included in the analysis.

In the hip and knee cohort, respectively, the mean (standard deviation) age was 72.6 (7.5) and 72.3 (7.2) years and 61.2 and 56.8% were female (Table 1). The prevalence of frailty was lower among cases compared with controls. For example, in the hip cohort, the prevalence of severe frailty was 3.6% among cases and 7.0% among controls, with similar results in the knee cohort (Table 1).

Table 2. Crude mortality at 30, 60 and 90 days following total hip arthroplasty and TKA

	30 days				60 days				90 days			
	THA		TKA		THA		TKA		THA		TKA	
	Number of deaths	Mortality, % (95% CI)	Number of deaths	Mortality, % (95% CI)	Number of deaths	Mortality, % (95% CI)	Number of deaths	Mortality, % (95% CI)	Number of deaths	Mortality, % (95% CI)	Number of deaths	Mortality, % (95% CI)
Frailty category												
Fit	109	0.25 (0.21, 0.30)	71	0.16 (0.13, 0.21)	137	0.32 (0.27, 0.38)	99	0.23 (0.19, 0.28)	166	0.39 (0.34, 0.46)	133	0.31 (0.27, 0.37)
Mild frailty	101	0.23 (0.19, 0.28)	125	0.22 (0.18, 0.26)	166	0.39 (0.34, 0.45)	168	0.30 (0.26, 0.35)	219	0.52 (0.46, 0.59)	197	0.35 (0.31, 0.41)
Moderate frailty	77	0.49 (0.39, 0.61)	72	0.32 (0.25, 0.40)	116	0.76 (0.63, 0.91)	107	0.48 (0.40, 0.58)	153	1.01 (0.86, 1.18)	136	0.62 (0.52, 0.73)
Severe frailty	32	0.85 (0.60, 1.20)	23	0.44 (0.29, 0.66)	45	1.22 (0.91, 1.64)	31	0.60 (0.42, 0.86)	50	1.37 (1.04, 1.81)	40	0.79 (0.58, 1.07)
Sex												
Women	147	0.23 (0.19, 0.26)	148	0.20 (0.17, 0.24)	232	0.36 (0.32, 0.41)	194	0.27 (0.24, 0.31)	290	0.46 (0.41, 0.51)	235	0.33 (0.29, 0.38)
Men	172	0.42 (0.36, 0.48)	143	0.26 (0.22, 0.30)	232	0.57 (0.50, 0.65)	211	0.39 (0.34, 0.44)	298	0.75 (0.67, 0.83)	271	0.50 (0.45, 0.57)
Age group (years)												
60–64	20	0.10 (0.06, 0.15)	13	0.05 (0.03, 0.09)	28	0.14 (0.10, 0.20)	23	0.10 (0.06, 0.15)	35	0.18 (0.13, 0.25)	29	0.12 (0.09, 0.18)
65–69	25	0.11 (0.07, 0.16)	34	0.12 (0.08, 0.16)	36	0.16 (0.12, 0.22)	46	0.16 (0.12, 0.22)	41	0.18 (0.14, 0.25)	56	0.20 (0.15, 0.26)
70–74	29	0.12 (0.09, 0.18)	37	0.13 (0.09, 0.17)	45	0.20 (0.15, 0.26)	52	0.18 (0.14, 0.24)	78	0.34 (0.27, 0.43)	70	0.24 (0.19, 0.31)
75–79	82	0.40 (0.32, 0.50)	63	0.25 (0.19, 0.32)	121	0.60 (0.50, 0.72)	94	0.38 (0.31, 0.46)	150	0.76 (0.64, 0.89)	120	0.49 (0.41, 0.58)
80–84	77	0.59 (0.47, 0.73)	78	0.53 (0.43, 0.67)	118	0.92 (0.77, 1.10)	107	0.75 (0.62, 0.90)	146	1.15 (0.98, 1.35)	126	0.89 (0.75, 1.06)
85–89	66	1.25 (0.98, 1.59)	47	0.89 (0.67, 1.19)	92	1.79 (1.46, 2.19)	61	1.19 (0.92, 1.52)	111	2.18 (1.81, 2.63)	82	1.61 (1.30, 2.00)
≥90	20	2.05 (1.32, 3.17)	19	3.00 (1.92, 4.10)	24	2.51 (1.68, 3.75)	22	3.58 (2.35, 5.43)	27	2.86 (1.96, 4.17)	23	3.79 (2.52, 5.70)
Quintile of IMD												
1 (least deprived)	74	0.26 (0.21, 0.33)	71	0.23 (0.18, 0.29)	102	0.37 (0.30, 0.45)	92	0.30 (0.24, 0.37)	132	0.48 (0.41, 0.57)	112	0.37 (0.31, 0.44)
2	71	0.27 (0.22, 0.35)	61	0.20 (0.16, 0.26)	110	0.43 (0.36, 0.52)	89	0.30 (0.24, 0.37)	140	0.56 (0.47, 0.66)	113	0.38 (0.32, 0.46)
3	79	0.34 (0.28, 0.43)	60	0.22 (0.17, 0.28)	115	0.51 (0.43, 0.61)	82	0.30 (0.24, 0.37)	143	0.64 (0.55, 0.76)	103	0.38 (0.31, 0.46)
4	51	0.29 (0.22, 0.39)	43	0.19 (0.14, 0.26)	72	0.42 (0.34, 0.53)	66	0.31 (0.24, 0.39)	88	0.52 (0.42, 0.65)	85	0.40 (0.32, 0.49)
5 (most deprived)	44	0.36 (0.27, 0.49)	56	0.33 (0.25, 0.42)	65	0.55 (0.43, 0.70)	76	0.45 (0.36, 0.56)	85	0.73 (0.59, 0.90)	93	0.56 (0.45, 0.68)

Table 3. Hazard ratio for 30-, 60- and 90-day mortality by frailty category among people who have a THA or TKA

	HR for mortality (95% CI)					
	30 days		60 days		90 days	
	Model 1[1]	Model 2[2]	Model 1[1]	Model 2[2]	Model 1[1]	Model 2[2]
	THA					
Fit	1 (reference)					
Mild frailty	1.19 (0.90, 1.56)	0.87 (0.66, 1.15)	1.57 (1.25, 1.97)	1.16 (0.92, 1.47)	1.66 (1.36, 2.04)	1.25 (1.02, 1.54)
Moderate frailty	3.13 (2.31, 4.25)	1.73 (1.26, 2.38)	3.82 (2.95, 4.94)	2.16 (1.65, 2.83)	3.95 (3.15, 4.97)	2.30 (1.81, 2.92)
Severe frailty	6.43 (4.26, 9.72)	2.85 (1.84, 4.39)	7.37 (5.18, 10.49)	3.37 (2.33, 4.88)	6.30 (4.53, 8.75)	2.99 (2.12, 4.21)
	TKA					
Fit	1 (reference)					
Mild frailty	1.70 (1.26, 2.28)	1.31 (0.97, 1.77)	1.61 (1.25, 2.07)	1.28 (0.99, 1.65)	1.40 (1.12, 1.75)	1.12 (0.89, 1.40)
Moderate frailty	2.93 (2.09, 4.11)	1.73 (1.22, 2.46)	3.04 (2.29, 4.04)	1.90 (1.41, 2.55)	2.86 (2.23, 3.66)	1.81 (1.40, 2.34)
Severe frailty	4.56 (2.81, 7.38)	2.14 (1.29, 3.53)	4.25 (2.80, 6.43)	2.16 (1.40, 3.32)	4.04 (2.81, 5.81)	2.10 (1.44, 3.07)

[1]Model 1 is adjusted for year of surgery only. [2]Model 2 is adjusted for year of birth, sex, IMD and year of surgery.

Crude 30-, 60- and 90-day mortality following THA and TKA

Among those who had a THA, the number of people who died: within 30 days was 319 (0.31%); within 60 days was 464 (0.45%) and within 90 days was 588 (0.57%). The corresponding deaths among TKA cases were: 30 days, 291 (0.23%); 60 days, 405 (0.32%) and 90 days, 506 (0.40%). Cause-specific 30-day mortality following THA and TKA is shown in Supplementary Table 3 (Supplementary data are available in *Age and Ageing* online). Among cases, diseases of the circulatory system, including heart disease and stroke, were the most common causes of death. There were substantial differences between cases and controls in the proportion of deaths due to neoplasms: among controls, about one-third of deaths were due to neoplasms, while among cases, only 2% were due to neoplasms. The hazard function (deaths per day) among cases who had a THA and TKA peaked in the early postoperative period, then declined during the remainder of the 90 day period following surgery (Supplementary Figure 1, Supplementary data are available in *Age and Ageing* online).

Among those who had joint surgery, mortality at 30, 60 and 90 days was higher in men than women and increased with increasing frailty and also with increasing age following both THA and TKA (Table 2).

Influence of frailty on short-term mortality following THA and TKA

Among those who had joint surgery, in a model adjusted for sex, age group, quintile of IMD and year of surgery, the HR for 30, 60 and 90 day mortality increased with increasing frailty in both the knee and hip cohorts. Compared with fit individuals, the adjusted HR (95% CI) for 30-day mortality following THA for mild, moderate and severely frail individuals, respectively, was 0.87 (0.66, 1.15), 1.73 (1.26, 2.38) and 2.85 (1.84, 4.39) (Table 3). The corresponding results following TKA were 1.31 (0.97, 1.77), 1.73 (1.22, 2.46) and 2.14 (1.29, 3.53). Similar results were observed at 60 and 90 days.

A multivariable logistic model predicting 30-day mortality following THA and TKA (with frailty category, 5-year age band, sex, year of surgery and quintile of IMD included as covariates) showed good discriminative ability (area under ROC curve: 0.81 for THA and 0.78 for TKA). There was variation in the predicted probability of 30-day mortality following THA and TKA in men and women by age band and frailty category (Table 4). The predicted probability (95% CI) of 30-day mortality following THA among fit men aged 60–64 years was 0.13% (0.06, 0.20), while the corresponding value for severely frail men aged ≥90 years was 6.55% (2.99, 10.11).

Influence of total hip and knee arthroplasty on short-term mortality

In a multivariable model adjusted for frailty category, age category, sex, quintile of IMD and year of surgery, the overall HR (95% CI) for mortality at 30, 60 and 90 days, respectively, among those who had THA compared with controls, was 1.05 (0.91, 1.23), 0.82 (0.73, 0.92) and 0.68 (0.62, 0.76). The corresponding results among cases who had TKA, compared with controls, was: 30 days, 1.14 (0.97, 1.34); 60 days, 0.83 (0.74, 0.95); and 90 days, 0.70 (0.63, 0.78). Mortality, however, varied by frailty status. In an adjusted model, mortality was increased at 30 days among fit cases compared with fit controls in both the hip and knee cohorts, respectively, 1.60 (1.15, 2.21) and 2.98 (1.81, 4.89) (Table 5). There was no statistically significant difference in 30-day mortality among mild, moderate and severe frail cases compared with controls in the same frailty category in both the hip and knee cohorts (Table 5). At 90 days following THA and TKA, mortality was reduced among cases with mild, moderate and severe frailty compared with controls in the same frailty category (Table 5). The effect was more marked among the severely frail group.

Table 4. Predicted probability of 30-day mortality following hip and knee arthroplasty in men and women, by age and frailty

Age group	Fit	Mild frailty		Moderate frailty		Severe frailty	
	Predicted probability of 30-day mortality, % (95% CI)[1]						
	THA						
	Women	*Men*	*Women*	*Men*	*Women*	*Men*	*Women*	*Men*
60–64	0.05 (0.03, 0.08)	0.13 (0.06, 0.2)	0.05 (0.02, 0.07)	0.11 (0.05, 0.17)	0.09 (0.04, 0.14)	0.23 (0.10, 0.35)	0.15 (0.06, 0.24)	0.37 (0.14, 0.60)
65–69	0.06 (0.03, 0.09)	0.14 (0.08, 0.21)	0.05 (0.03, 0.08)	0.13 (0.07, 0.19)	0.10 (0.05, 0.15)	0.25 (0.12, 0.38)	0.16 (0.07, 0.26)	0.41 (0.17, 0.64)
70–74	0.06 (0.03, 0.10)	0.16 (0.09, 0.23)	0.06 (0.03, 0.08)	0.14 (0.08, 0.20)	0.11 (0.06, 0.17)	0.28 (0.15, 0.41)	0.18 (0.08, 0.29)	0.45 (0.20, 0.71)
75–79	0.20 (0.12, 0.28)	0.50 (0.32, 0.68)	0.18 (0.11, 0.24)	0.44 (0.28, 0.59)	0.35 (0.22, 0.48)	0.86 (0.55, 1.18)	0.57 (0.30, 0.84)	1.4 (0.75, 2.05)
80–84	0.29 (0.18, 0.41)	0.73 (0.45, 1.01)	0.26 (0.16, 0.35)	0.64 (0.41, 0.87)	0.51 (0.32, 0.7)	1.26 (0.80, 1.72)	0.83 (0.45, 1.21)	2.04 (1.11, 2.96)
85–89	0.60 (0.35, 0.84)	1.47 (0.88, 2.06)	0.53 (0.32, 0.73)	1.29 (0.80, 1.78)	1.04 (0.65, 1.42)	2.53 (1.59, 3.46)	1.68 (0.93, 2.43)	4.06 (2.27, 5.86)
≥90	0.99 (0.44, 1.53)	2.41 (1.1, 3.71)	0.87 (0.41, 1.33)	2.12 (1.01, 3.24)	1.70 (0.82, 2.59)	4.11 (2.01, 6.22)	2.75 (1.22, 4.29)	6.55 (2.99, 10.11)
	TKA							
	Women	*Men*	*Women*	*Men*	*Women*	*Men*	*Women*	*Men*
60–64	0.03 (0.01, 0.05)	0.05 (0.02, 0.08)	0.04 (0.02, 0.07)	0.06 (0.02, 0.10)	0.05 (0.02, 0.09)	0.08 (0.03, 0.14)	0.06 (0.02, 0.11)	0.10 (0.03, 0.17)
65–69	0.06 (0.03, 0.10)	0.10 (0.05, 0.15)	0.09 (0.05, 0.12)	0.13 (0.07, 0.19)	0.11 (0.06, 0.17)	0.17 (0.09, 0.26)	0.13 (0.05, 0.21)	0.21 (0.08, 0.33)
70–74	0.06 (0.03, 0.09)	0.10 (0.05, 0.15)	0.09 (0.05, 0.12)	0.13 (0.07, 0.19)	0.11 (0.06, 0.16)	0.17 (0.09, 0.25)	0.13 (0.05, 0.21)	0.21 (0.08, 0.33)
75–79	0.12 (0.07, 0.17)	0.18 (0.10, 0.26)	0.16 (0.10, 0.22)	0.24 (0.15, 0.33)	0.2 (0.12, 0.29)	0.32 (0.19, 0.45)	0.24 (0.11, 0.37)	0.37 (0.17, 0.58)
80–84	0.25 (0.14, 0.36)	0.39 (0.22, 0.55)	0.33 (0.21, 0.46)	0.51 (0.32, 0.70)	0.44 (0.27, 0.60)	0.67 (0.41, 0.94)	0.52 (0.25, 0.78)	0.80 (0.38, 1.21)
85–89	0.42 (0.22, 0.61)	0.64 (0.34, 0.94)	0.55 (0.32, 0.78)	0.85 (0.49, 1.21)	0.72 (0.42, 1.03)	1.11 (0.64, 1.59)	0.86 (0.40, 1.31)	1.32 (0.60, 2.03)
≥90	1.47 (0.60, 2.35)	2.26 (0.93, 3.59)	1.95 (0.89, 3.02)	2.99 (1.37, 4.61)	2.55 (1.17, 3.92)	3.88 (1.79, 5.98)	3.00 (1.18, 4.82)	4.56 (1.79, 7.33)

[1]Predicted probabilities of 30-day mortality were calculated at the median values of quintile of IMD (which was 3) and year of surgery (which was 2010).

There were small differences in the mean eFI between cases and controls in the same frailty category (Supplementary Table 4, Supplementary data are available in *Age and Ageing* online). However, a sensitivity analysis adjusting additionally for the eFI score as a continuous measure did not materially impact on the results (Supplementary Table 5, Supplementary data are available in *Age and Ageing* online). Among cases and controls in the same frailty category, there were differences in the prevalence of some of the individual deficits that make up the eFI, however, adjusting for each of the individual deficits of the eFI in a sensitivity analysis did not materially impact on the results (Supplementary Table 6, Supplementary data are available in *Age and Ageing* online).

Modelling deaths due to causes other than neoplasms among cases and controls, with deaths due to neoplasms modelled as competing risks, was associated with a small increase in mortality among cases compared with controls in each frailty strata compared with analysis looking at all-cause mortality, though the gradient of risk across the frailty strata was similar (Supplementary Table 7, Supplementary data are available in *Age and Ageing* online).

Discussion

In this study, the hazard ratio for 30-, 60- and 90-day mortality increased with increasing frailty following THA and TKA. The probability of 30-day mortality following THA varied by age, gender and frailty; from 0.05% among non-frail women aged 60–64 years to 6.55% among severely frail men aged ≥90. The hazard ratio for mortality among cases compared with controls varied by frailty. All-cause mortality was increased in fit cases compared with fit controls at 30 days in both the hip and knee cohorts, though by 90 days, there was no statistically significant difference. Among cases with mild, moderate or severe frailty compared with controls in the same frailty strata, there was no statistically significant difference in all-cause mortality at 30 days in both the hip and knee cohorts and reduced mortality at 60 and 90 days.

Previous studies, all from the USA, have consistently demonstrated increased mortality up to 90 days following THA and TKA with increasing frailty [3–9]. Direct comparison with our study is difficult due to differences in the assessment of frailty. In one study of 8,640 individuals who had a primary or revision THA [median age (inter quartile range) 68 (60, 76) years], frailty was assessed using a 32-component frailty index and categorised as non-frail (FI < 0.11), vulnerable (0.11 ≤ FI < 0.20) and frail (FI ≤ 0.21) [4]. In an adjusted model, the HR (95% CI) for 90-day mortality among those who were vulnerable and frail, respectively, was 2.31 (0.89, 6.18) and 5.61 (2.24, 14.03), compared with those who were non-frail [4]. These results are similar to our findings, though the relationship between frailty and 90-day mortality following THA was less strong in our study. These differences may potentially be explained by differences in the cohort (we did not include revision surgery in our study) and differences in the thresholds for frailty categories.

Table 5. Hazard ratio for 30-, 60- and 90-day mortality among cases compared with controls, by frailty category

Frailty category	HR for mortality among cases versus controls (95% CI) [1]					
	30 days		60 days		90 days	
	Hip cohort	Knee cohort	Hip cohort	Knee cohort	Hip cohort	Knee cohort
Fit	1.60 (1.15, 2.21)	2.98 (1.81, 4.89)	1.07 (0.83, 1.39)	1.71 (1.22, 2.41)	0.83 (0.67, 1.03)	1.38 (1.05, 1.81)
Mild frailty	0.90 (0.69, 1.17)	1.27 (0.97, 1.66)	0.79 (0.65, 0.97)	0.94 (0.76, 1.16)	0.64 (0.54, 0.76)	0.71 (0.59, 0.85)
Moderate frailty	0.99 (0.74, 1.33)	0.82 (0.61, 1.10)	0.77 (0.62, 0.97)	0.67 (0.53, 0.85)	0.71 (0.59, 0.87)	0.59 (0.48, 0.73)
Severe frailty	0.88 (0.58, 1.34)	0.68 (0.42, 1.10)	0.65 (0.46, 0.91)	0.44 (0.29, 0.65)	0.52 (0.38, 0.71)	0.40 (0.28, 0.56)

[1]Results calculated by considering a statistical interaction term between case/control status and frailty category to estimate HR for mortality in cases compared with controls in the same strata of frailty. Adjusted for year of birth, sex, and IMD and year of surgery of case.

The explanation for reduced all-cause mortality at 90-days among people with mild, moderate and severe frailty who have a THA or TKA compared with controls in the same frailty category is not clear. It is likely that there may have been a residual healthy surgery effect, with those listed for surgery relatively fitter than those who were not listed for surgery [1], despite accounting for frailty category in our analyses. The greater reduction in mortality among the severely frail group who had surgery compared with severely frail controls would be consistent with this; also the relatively fewer number of deaths due to neoplasia among those who had surgery compared with controls. After accounting for the differential mortality due to neoplasia, there was a small increase in the risk of mortality (among cases compared with controls) though the gradient of risk across the frailty strata was similar. It is possible though also that interventions in preparation for surgery, related for example to prehabilitation, pre-operative assessment and also increased monitoring and care following surgery, may have had a beneficial impact on reducing mortality among those with higher frailty scores who had joint surgery compared with those who had not had surgery.

Our study has a number of strengths, including a large sample size, linkage to secondary care and national mortality data, and the use of a well validated frailty index. There are also limitations to our analysis. A key limitation is in the analysis of short-term mortality following THA/TKA relative to a non-surgical control population, with a likely residual 'health selection effect', resulting in relatively fitter cases relative to non-surgical controls, despite accounting for frailty in our analysis. We attempted to account for residual imbalance in frailty status between cases and controls in the same frailty category by adjusting for the eFI as a continuous measure and also adjusting for each of the 36 deficits of the eFI. However, it is likely that residual imbalance persisted, which is difficult to address completely using routinely collected coded clinical data. Other factors which impact on who is selected for surgery which are not well captured in routine clinical records, such as OA disease severity, severity of co-morbidities and patient willingness to undergo surgery, may result in residual confounding if these factors also influence the outcome. In particular, robust measures of the severity of the individual deficits which make up the eFI were not available to us, so individuals with the same eFI score and the same underlying deficits may differ in the severity of their co-morbidities.

In summary, in this study using data from the UK, short-term mortality increased with increasing frailty following THA and TKA. The predicted probability of 30-day mortality following surgery varied by age, gender and frailty status, in the case of THA from 0.05% to 6.5%. Among those with frailty, the reduction in mortality at 60 and 90 days following THA/TKA compared with controls who did not have surgery may be due to a healthy surgery effect which could in part be explained by a reduction in deaths due to neoplasia.

Supplementary Data: Supplementary data mentioned in the text are available to subscribers in *Age and Ageing* online.

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