

# BMJ Open Increased early mortality after total knee arthroplasty using conventional instrumentation compared with technology-assisted surgery: an analysis of linked national registry data

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## ABSTRACT

**Objectives** This study aims to compare early mortality after total knee arthroplasty (TKA) using conventional intramedullary instrumentation to TKA performed using technology-assisted (non-intramedullary) instrumentation.

**Design** Comparative observational study. Using data from a large national registry, the 30-day mortality after unilateral TKA performed for osteoarthritis was compared between procedures using conventional instrumentation and those using technology-assisted instrumentation. Firth logistic regression was used to calculate ORs, adjusting for age, sex, use of cement and procedure year for the whole period, and additionally adjusting for American Society of Anesthesiologists physical status classification system class and body mass index (BMI) for the period 2015 to 2019. This analysis was repeated for 7-day and 90-day mortality.

**Setting** National arthroplasty registry.

**Participants** People undergoing unilateral, elective TKA for osteoarthritis from 2003 to 2019 inclusive.

**Interventions** TKA performed using conventional intramedullary instrumentation or technology-assisted instrumentation.

**Main outcome measures** 30-day mortality (primary), and 7-day and 90-day mortality.

**Results** A total of 581 818 unilateral TKA procedures performed for osteoarthritis were included, of which 602 (0.10%) died within 30 days of surgery. The OR of death within 30 days following TKA performed with conventional instrumentation compared with technology-assisted instrumentation, adjusted for age, sex, cement use, procedure year, American Society of Anesthesiologists and BMI was 1.72 (95% CI, 1.23 to 2.41,  $p=0.001$ ). The corresponding ORs for 7-day and 90-day mortality were 2.21 (96% CI, 1.34 to 3.66,  $p=0.002$ ) and 1.35 (95% CI, 1.07 to 1.69,  $p=0.010$ ), respectively.

**Conclusions** The use of conventional instrumentation during TKA is associated with higher odds of early postoperative death than when technology-assisted instrumentation is used. This difference may be explained by complications related to fat embolism secondary to intramedullary rods used in conventional instrumentation. Given the high number of TKA performed annually

## STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ Use of national linked data.
- ⇒ Large sample size.
- ⇒ Adjustment for known likely confounders.
- ⇒ Observational study design (possible unmeasured confounders).

worldwide, increasing the use of technology-assisted instrumentation may reduce early post-operative mortality.

## INTRODUCTION

Total knee arthroplasty (TKA) is a common procedure for severe osteoarthritis of the knee, with an average annual rate of 135 per 100 000 population in contributing Organization for Economic Cooperation and Development (OECD) countries and 226 per 100 000 in Australia.<sup>1,2</sup> Conventional instrumentation for TKA surgery requires the insertion of a long intramedullary rod into the femur (and sometimes the tibia) which is then used as a reference for alignment of the cutting blocks applied to the bone for prosthesis preparation. This insertion creates fat and bone marrow embolisation, as shown by transthoracic echocardiography and analysed by biopsy.<sup>3</sup> The embolic material may produce fat embolism syndrome, which includes respiratory, cardiac, haematological and neurological complications and sudden death.<sup>4-6</sup> Over the last two decades, three new techniques have been introduced that allow alignment to be referenced without intramedullary instrumentation. These technology-assisted instrumentation techniques are computer navigation, image-derived instrumentation and robotic assistance. Although these techniques were developed to improve postoperative alignment, evidence for this is variable.

Computer navigation has demonstrated improved alignment compared with standard instruments, however, there is mixed evidence that revision rates or patient-reported outcomes are superior using this technique.<sup>7–13</sup> However, trials comparing any of these newer techniques to conventional instrumentation were underpowered to detect early mortality postoperatively, which has been decreasing over time (possibly due to improvements in operative and perioperative management) and is currently approximately 0.1% at 30 days.<sup>14 15</sup>

This study aims to compare the 30-day all-cause mortality after TKA between procedures performed using conventional intramedullary instrumentation to those performed using technology-assisted instrumentation using data from a large national registry.

## METHODS

The Australian Orthopaedic Association National Joint Replacement Registry (AOANJRR) is a national registry with near complete (over 98%) coverage of TKA procedures performed in Australia since 2003.<sup>2</sup> AOANJRR data from January 2003 to December 2019 for patients undergoing unilateral TKA for osteoarthritis were used. Patients undergoing bilateral same-day primary TKA or any primary TKA within 90 days of a contralateral primary TKA were excluded. AOANJRR data include patient-identified data and surgical variables, which includes the use of assistive technology, and these data are linked to the National Death Index twice yearly to record fact and date of death. All data used in the analysis were available in the AOANJRR from inception except the American Society of Anesthesiologists (ASA) class<sup>16</sup> (a measure of comorbidity and mortality risk, available since 2012) and body mass index (BMI, available since 2015).

The increased mortality associated with TKA is maximal within 30 days but may extend to 90 days postsurgery.<sup>17 18</sup> Therefore, 30-day mortality was chosen as the primary outcome; 7-day and 90-day mortality were chosen as secondary outcomes. Age, sex, use of bone cement, ASA class and BMI were chosen as potential confounders due to their known association with mortality. Procedure year was added as a covariate due to the increase in the proportion of cases using technology-assisted instrumentation over time and, because 30-day mortality has been decreasing over time.<sup>14</sup>

Technology-assisted surgery was defined as any procedure using computer navigation, image derived instrumentation (IDI) or robotic assistance. Computer navigation involves the use of a tracking device, most commonly an infrared camera and a computer. Rigid reference arrays are attached to the patient and a registration process enables the software to determine the patient's anatomy and accurately track instruments to assist surgery. The surgeon then makes the appropriate bone cuts and monitors the alignment of the knee. Robotic assistance uses similar principles, but a robotic

arm guides the cutting tools to facilitate the surgery. Both these techniques allow intraoperative verification of the component position. IDI is the use of individualised custom-made 3D printed guides or cutting blocks derived from preoperative CT or MRI scans of the patient's knee. These guides or blocks are used to perform the required bone cuts and are specific to each patient's anatomy. Conventional instrumentation was defined as any procedure not using any of the technology-assisted methods. Cause of death was not used, as multiple causes are often reported, it may be inconsistently reported,<sup>19</sup> and it is less relevant than overall mortality.

Between-group differences in mortality were expressed as odds ratios (ORs), calculated by logistic regression adjusting for age, sex and procedure year. Due to low numbers of deaths, Firth logistic regression (which uses penalised likelihood) was used to avoid the small sample bias inherent in regression using conventional maximum likelihood estimation.<sup>20</sup> Adjusted mortality was obtained after direct standardisation of the crude cumulative mortality data, by 5-year age intervals and sex, to the Estimated Resident Population Status, based on the 2001 census. Interaction terms were tested for each covariate against instrumentation type.

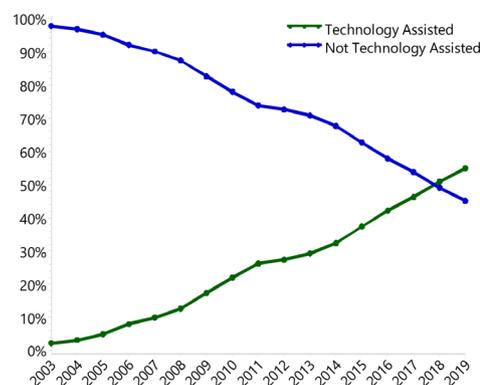
A secondary analysis of mortality adjusted for age, sex, procedure year, bone cement use, ASA and BMI was performed in the subset of procedures performed since 2015 (when ASA and BMI data were available). Fully adjusted analyses were repeated using 7-day and 90-day mortality as the outcome measures.

A sensitivity analysis was performed by restricting the population to patients who had only one primary TKA recorded in the AOANJRR, which excluded all patients with contralateral TKA.

As it was unlikely that patients died in another country within 30 or 90 days of surgery without registration of their death, an assumption of no missing data was made.

## Patient and public involvement

Patients or the public were not involved in the design, or conduct, or reporting, or dissemination plans of our research.



**Figure 1** The use of technology-assisted instrumentation over time for primary unilateral TKA. TKA, total knee arthroplasty.

**Table 1** Demographic data and use of technology-assisted surgery in patients undergoing unilateral TKA

	Technology-assisted surgery	Conventional surgery	Total
Mean age (SD) in years	68.5 (9.0)	69.1 (9.2)	69.0 (9.1)
Sex (proportion male)	43.3%	42.0%	42.4%
ASA class* (proportion)			
1	5.6%	5.2%	5.4%
2	53.8%	54.5%	54.2%
3	39.4%	39.1%	39.3%
4	1.2%	1.2%	1.2%
5	0.0%	0.0%	0.0%
Mean BMI† (SD)	32.0 (14.2)	32.3 (17.1)	32.2 (15.8)
Procedures	170 496	411 322	581 818

\*ASA class was available for 293 624 procedures.  
 †BMI was available for 213 259 procedures.  
 ASA, American Society of Anesthesiologists; BMI, body mass index; TKA, total knee arthroplasty.

## RESULTS

A total of 581 818 unilateral TKA procedures were included from 1 January 2003 to 31 December 2019. The increasing use of technology-assisted instrumentation over time is shown in [figure 1](#), and descriptive data of patient demographics and the use of technology-assisted surgery is provided in [table 1](#). Procedures using technology-assisted surgery comprised 129 179 computer navigation, 34 898 image-derived instrumentation, 7288 robotic assisted and 869 using a combination of technologies.

The distribution of deaths between groups for 30-day, and 7-day and 90-day postsurgical periods are provided in [tables 2 and 3](#), respectively. The OR of death within 30 days for TKA performed with conventional instrumentation compared with technology-assisted instrumentation, adjusted for age, sex, cement use and procedure year was 1.48 (95% CI, 1.19 to 1.85,  $p < 0.001$ ). For the subset of 212 937 procedures where ASA and BMI data were available, the OR adjusted for age, sex, procedure year, cement use, ASA and BMI was 1.72 (95% CI, 1.23 to 2.41,  $p = 0.001$ ). The corresponding (fully adjusted) ORs for 7-day and 90-day mortality were 2.27 (95% CI, 1.33 to 8.74,  $p = 0.002$ ) and 1.35 (95% CI, 1.07 to 1.69,  $p = 0.010$ ), respectively. The models for the fully adjusted analyses are shown in [table 4](#). Two-way interaction terms between age, sex, BMI, ASA class, cement use and procedure year and use of technology-assisted instrumentation were tested and found to be not significant.

The sensitivity analysis restricted to patients who had only one unilateral TKA recorded showed similar significant differences between technology assisted and conventional instrumentation, although the overall (and standardised) mortality was higher in this group (analyses not shown).

## DISCUSSION

### Statement of principal findings

The use of conventional instrumentation during unilateral TKA was associated with a significantly higher 30-day mortality when compared with technology-assisted instrumentation, allowing for differences in age, sex, cement use, ASA class, BMI and year of procedure.

### Strengths and weaknesses of the study

A strength of this study is the use of national data and the large sample size. Furthermore, adjusting for patient-level factors and procedure year, has accounted for differences in patient selection, improvements in perioperative management and the increasing use of technology-assisted instrumentation over time.

This study is limited by the possibility that the associations may be subject to residual confounding from unknown variables. Randomised trials to answer this question may not be feasible due to the very large sample size required due to the small event rate. Surgical times are

**Table 2** 30-day mortality following unilateral TKA for osteoarthritis

Group	Patients (n)	Deaths (n)	Deaths (%)	Standardised mortality
Conventional instrumentation	411 322	495	0.120	0.036
Technology-assisted instrumentation	170 496	107	0.063	0.018
Total	581 818	602	0.103	0.031

TKA, total knee arthroplasty.

**Table 3** 7-day and 90-day mortality following unilateral TKA for osteoarthritis

Group	Patients (n)	7-day mortality			90-day mortality		
		Deaths (n)	Deaths (%)	Standardised mortality	Deaths (n)	Deaths (%)	Standardised mortality
Conventional instrumentation	411 322	214	0.052	0.015	919	0.233	0.074
Technology-assisted instrumentation	170 496	38	0.022	0.005	240	0.141	0.043
Total	581 818	252	0.043	0.012	1159	0.199	0.065

TKA, total knee arthroplasty.

reported to be slightly longer when technology-assisted methods are used,<sup>21</sup> but this would not be expected to be associated with a reduction in mortality.

### Strengths and weaknesses in relation to other studies

The relative mortality of conventional and technology-assisted instrumentation in TKA has not been previously reported.

### Meaning of the study: possible explanations and implications for clinicians and policymakers

The difference in mortality based on the use of technology-assisted instrumentation has been recently reported (with stronger effect) for bilateral TKA<sup>22</sup> and may be related to the insertion of an intramedullary rod into the femur

(and in some cases, the tibia) during conventional instrumentation and the resulting fat embolism. Initial studies using non-invasive intraoperative ultrasound have demonstrated that there are less emboli with computer navigation compared with conventional instrumentation, although these studies were small.<sup>23 24</sup> However, later studies with larger study populations have shown that while avoiding intramedullary instrumentation does not significantly reduce the incidence of fat embolisation during TKA,<sup>25 26</sup> it may reduce the embolic load.<sup>27</sup> Cerebral fat embolism has also been reported after standard TKA,<sup>4 28</sup> but there is a lack of studies comparing technology-assisted and standard instrumented TKA. Alternatively, fat emboli may arise from other parts of the surgery such as impaction

**Table 4** Full regression model for mortality using data from 2015 to 2019, inclusive

Variable	30-day mortality		7-day mortality		90-day mortality	
	OR (95% CI)	P value	OR (95% CI)	P value	OR (95% CI)	P value
Conventional vs technology assisted	1.72 (1.23 to 2.43)	0.001	2.21 (1.34 to 3.66)	0.002	1.35 (1.07 to 1.69)	0.01
ASA class (ref=1)						
2	2.14 (0.43 to 10.66)	<0.001	1.10 (0.22 to 5.47)	0.91	1.52 (0.59 to 3.91)	0.001
3	4.68 (0.94 to 23.25)	0.07	1.89 (0.38 to 9.38)	0.44	3.33 (1.30 to 8.53)	0.08
4	16.62 (3.04 to 90.78)	0.19	4.23 (0.64 to 27.99)	0.07	12.07 (4.37 to 33.38)	0.07
5	419.4 (11.78 to 14934)	0.003	451.5 (13.69 to 14894)	<0.001	141.8 (5.11 to 3935)	0.02
Age (per year)	1.08 (1.06 to 1.10)	<0.001	1.08 (1.05 to 1.17)	0.01	1.08 (1.07 to 1.10)	0.01
BMI (ref=normal)						
Underweight	0.96 (0.56 to 1.64)	0.80	3.25 (0.20 to 53.22)	0.09	5.87 (2.38 to 14.51)	<0.001
Overweight	0.95 (0.51 to 1.77)	0.79	1.06 (0.47 to 2.37)	0.89	0.99 (0.69 to 1.42)	0.02
Obese class 1	1.25 (0.63 to 2.48)	0.55	1.23 (0.54 to 2.81)	0.62	0.88 (0.61 to 1.29)	0.002
Obese class 2	0.93 (0.55 to 1.56)	0.70	1.25 (0.49 to 3.19)	0.65	0.89 (0.57 to 1.38)	0.01
Obese class 3	1.12 (0.07 to 18.12)	0.94	2.50 (0.95 to 6.57)	0.06	1.06 (0.65 to 1.75)	0.26
Procedure year (per year)	1.06 (0.94 to 1.18)	0.35	0.97 (0.83 to 1.14)	0.73	1.02 (0.95 to 1.11)	0.57
Female (vs male)	0.63 (0.46 to 0.87)	0.004	0.52 (0.33 to 0.83)	0.005	0.62 (0.50 to 0.78)	<0.001
No cement (vs cement)	1.89 (1.15 to 3.09)	<0.001	1.84 (0.92 to 3.67)	0.09	1.35 (0.91 to 2.00)	0.14

ASA, American Society of Anesthesiologists; BMI, body mass index.

of the femoral and tibial implants, but this is unlikely to differ between technology-assisted and conventionally instrumented TKA.<sup>25–27</sup>

The higher 30-day mortality associated with cementless fixation may also be related to fat emboli due to potential higher impaction forces used in cementless fixation. This association has not previously been reported, however a recent study from the Dutch arthroplasty register showed that the OR for 30-day mortality in cementless fixation compared with cemented fixation was 1.46 (95% CI, 0.74 to 2.90). This difference was not statistically significant but used a smaller sample than that used in the current study.<sup>29</sup>

Stein *et al* examined over 900 million patients using data from the US National Hospital Discharge Survey from 1979 to 2005 and reported 41 000 patients (0.004%) with fat embolism syndrome.<sup>30</sup> They stated that the incidence of fat embolism with lower limb joint replacement was too low to calculate accurately. However, it is possible that cases of sudden death associated with surgery were not diagnosed as fat embolism syndrome.<sup>4 31</sup>

Another possible cause for the observed difference in mortality is perioperative blood loss. Although blood loss was not measured in this study, previous research has shown surgical blood loss is lower with technology-assisted knee surgery.<sup>32 33</sup> This factor may affect mortality directly or by reducing the need for blood transfusion.

Although the ORs for the associations were lower for 90-day mortality, the 90-day mortality is higher, such that the difference likely relates to a similar risk difference. The higher OR for 7-day compared with 30-day mortality, and 30-day compared with 90-day mortality suggests that the largest difference in mortality occurs in the early post-operative period. Mortality after TKA has fallen over the last few decades and the current 30-day mortality after TKA is approximately 0.1%.<sup>14 15</sup> Given the low event rate for death post-TKA, the ORs found in this analysis can be approximated as risk ratios. This suggests that the use of conventional instrumentation is associated with a 72% increase in 30-day mortality after TKA when compared with assistive technology use. It is estimated that approximately one million TKA are performed in the USA annually with that rate expected to rise significantly up to 2050.<sup>34 35</sup> Globally, assuming over two million cases are performed annually,<sup>36</sup> if the difference in mortality is due to the use of conventional instrumentation, the use of technology-assisted instrumentation would result in approximately 1000 fewer deaths per year, depending on the current rate of technology-assisted instrumentation.

### Unanswered questions and future research

This study should be replicated using large data sets and joint registries from other regions that collect data on technology-assisted TKA. If verified, this finding has a major implication for the conduct of TKA surgery worldwide. While there is little clinical disadvantage to using technology-assisted surgery, there is an increased cost.

Future research may determine the cost effectiveness of using technology-assisted instrumentation.

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**Contributors** IAH contributed to study concept, design, analysis, interpretation and drafted the manuscript and is guarantor of the study. IAH, DPK, YP, PLL, RSdS and SEG have approved the final version of the manuscript and agree to be accountable for the work. DPK contributed to concept, interpretation and revising the manuscript. YP conducted the statistical analysis and revised the manuscript. PLL and RSdS contributed to study design, interpretation and manuscript revision. SEG contributed to study design, interpretation and manuscript revision.

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**Competing interests** None declared.

**Patient and public involvement** Patients and/or the public were not involved in the design, or conduct, or reporting or dissemination plans of this research.

**Patient consent for publication** Not required.

**Ethics approval** This study involves human participants. The AOANJRR is approved by the Commonwealth of Australia as a federal quality assurance activity (QAA 3/2017) under Part VC of the Health Insurance Act, 1973. All AOANJRR studies are conducted in accordance with ethical principles of research (the Helsinki Declaration II). Consent waiver applies to the registry from which data were obtained.

**Provenance and peer review** Not commissioned; externally peer reviewed.

**Data availability statement** Data are available upon reasonable request. Data are held by the Australian Orthopaedic Association National Joint Replacement Registry and are available on request subject to conditions. External access to and use of deidentified AOANJRR data must be in accordance with AOANJRR policies (Ref No POL.S3.3, S3.4, S3.5) available on the registry website: <https://aoanjrr.sahmri.com/policies>. Requests for data use can be made by contacting the AOANJRR Manager: Telephone +61 8128 4284, Email [cturner@aoanjrr.org.au](mailto:cturner@aoanjrr.org.au).

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