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ORIGINAL PAPER

Implementation of robotic-assisted total knee arthroplasty in the public health system: a comparative cost analysis

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Abstract

Purpose Robotic-assisted total knee arthroplasty (TKA) may improve the precision of bone preparation and component alignment when compared to the conventional surgical approach; however, the detailed cost analysis of robotic-assisted TKA is lacking. This study aims to compare in-hospital costs between robotic-assisted and computer-navigated TKA.

Methods Patients undergoing primary TKA at a public hospital in Sydney between October 2018 and June 2019 were included. Patient demographics, surgical outcomes and in-hospital cost variables including, staff, critical care, emergency department, diagnostic, prosthesis, operating room, ward and other related costs until the discharge to the community were collected. Differences across in-hospital costs between robotic-assisted and computer-navigated TKA were compared using independent Student's *t*-tests.

Results Of the 258 primary TKAs, 181 (70.2%) were computer-navigated and 77 (29.8%) robotic-assisted. Surgical time ($p<0.001$) and operating time ($p<0.001$) were both significantly shorter in computer-navigated TKA, while robotic-assisted TKA cases were more likely to be discharged directly home without extended in-patient rehabilitation ($p=0.014$). When removing the capital costs of surgical equipment and maintenance, there was no difference in total in-hospital cost between computer-navigated ($19,512.3) and robotic-assisted TKA ($18,347.1; $p=0.179$). When these capital costs were included, the mean in-hospital cost of robotic-assisted surgery was $21,507.6 compared to $19,659.7 for computer-navigated TKA ($p=0.034$).

Conclusions The total in-hospital cost, during the implementation period of robotic-assisted TKA, is comparable with computer-navigated TKA. Robotic-assisted TKA was significantly more expensive when the upfront cost of the robotic system and maintenance costs were included. Longer term cost benefit of robotic-assisted TKA should be investigated in future studies.

Keywords Total knee arthroplasty · Robotic assisted · Computer navigated · Cost

Introduction

Joint replacement is the gold standard treatment for patients presenting with advanced degenerative and inflammatory disease of the knee who have failed to respond to conservative treatment [1, 2]. Conventional knee arthroplasty performed with manual instrumentation is the most common surgical technique for performing the knee replacement in these patients, with computer-aided surgery gradually increasing in utilisation and more recently robotic-assisted techniques being introduced [3].

While acceptable overall long-term survivorship has been reported with manual and computer-navigated instrument techniques, there remains a proportion of patients who go on

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to early revision, and up to 20% of patients reporting dissatisfaction with their TKA [4, 5]. In addition, the cost benefit of computer navigated is more likely in high volume centres [6], given an additional cost of US$ 800 to US$ 1500 per operation when compared to mechanical alignment systems [7, 8]. This has driven the ongoing development of techniques aimed at improving accuracy and repeatability of the surgery, with the goal of translation into improved implant longevity, survivorship and patient functional performance. With the rapid advancement of technology, robotic-assisted surgery (RAS) has gained popularity [9, 10].

Recent studies have compared computer-navigated technique with the newly developed robotic technology, wherein robotic-assisted total knee arthroplasty (TKA) demonstrated superiority over computer-navigated surgery in the precision of bone preparation and component alignment [11, 12]. These radiographic advantages of RAS over computer-navigated TKA are thought to improve postoperative pain and functional outcomes, although the evidence remains limited [13]. Cost plays a significant role in the implementation and uptake of any new surgical technology, and its consideration is critical when evaluating the cost–benefit analysis to the community which is ultimately funding the provision of health care. Consequently, a greater understanding of the costs associated with robotic-assisted TKA, especially during the early implementation phase, is needed.

A limited number of studies have explored the difference in costs between robotic-assisted and computer-navigated TKA [14, 15]. Cool et al. [15] compared 90-day episode of care costs and found robotic-assisted TKA (US$ 18,568) had lower episode costs than conventional TKA (US$ 20,960) [15]. Some of the main contributors highlighted as reducing the cost of robotic-assisted TKA were shorter length of hospital stay, greater likelihood of being discharged home and lower re-admission rates. Similarly, a study investigating the cost of robotic-assisted unicompartmental knee arthroplasty (UKA) compared to conventional UKA found robotic-assisted UKA was considered cost-effective when the number of surgeries exceeded 94 cases per year [16]. It was noted there was a critical difference in these studies regarding whether the upfront costs of the robotic-assisted equipment and the associated ongoing maintenance fees were included in the analysis. This is an important consideration, as it provides a more accurate cost of the implementation of new technology.

Given these differences in approach, it is evident a detailed cost investigation comparing robotic-assisted and computer-navigated primary TKA, including the upfront capital equipment investment and its associated service cost, would provide valuable information to clinicians, health organisations and patients. Thus, the purpose of this study was to detail and compare the initial in-hospital cost between robotic-assisted and computer-navigated primary TKA.

Materials and methods

This study followed the Strengthening of Reporting Observational Studies in Epidemiology (STROBE) guidelines [17].

Study design and setting

This study is a retrospective cohort of routinely collected cost and clinical data from all primary TKAs performed at Royal Prince Alfred Hospital, Sydney (RPAH), Australia, from October 2018 to June 2019. Ethics approval was granted by the Sydney Local Health District Human Ethics Committee (X19-0456, HREC number: 2019/ETH13554).

Participants

Consecutive patients, aged 18 years or older undergoing primary TKA due to degenerative joint disease, were included. The study group consisted of patients that underwent robotic-assisted TKA with Stryker's MAKO™ System and the comparator group consisted of patients that underwent computer-navigated TKA with Stryker's ASM system. Both robotic-assisted and computer-navigated procedures were undertaken within the same time period by five experienced surgeons within RPAH. Patients that underwent limb-sparing mega-arthroplasty were excluded. The decision to perform robotic or computer-navigated TKA was made by each of the individual orthopaedic surgeons, without any specific generalised criteria. Furthermore, the alignment strategy was based on the surgeon's preference and included mechanical alignment, kinematic, gap balancing and hybrid techniques. The amount of hospital staff in the operation room during the procedures varied between six to eight staff members. These are normally composed of orthopaedic surgeon, registrar/fellow (usually both), anaesthetist, anaesthetic nurse, instrument nurse, and circulating nurse (usually 2). The number of staff members was constant across robotic-assisted and computer-navigated TKAs.

Outcomes of interest

The cost information was provided by the Sydney Local Health District Performance Unit. Patient characteristics (i.e. age, gender, BMI, ASA, country of birth, place of residence, health insurance status and diagnosis) and surgical outcomes (i.e. surgical time, length of hospital stay, discharge destination and hospital re-admission within 28 days) were extracted from the institutional prospective clinical database (Lower Limb Arthroplasty Database—LOAD).

Total in-hospital cost

The total in-hospital cost of each patient episode was calculated from admission to hospital discharge using inpatient fraction of costs (IFRAC) [18]. This is an initial top-down costing methodology examining the expenses of each cost centre, grouping them into cost pools, which are then allocated down to services. These costs are then refined by a bottom-up approach. This included the following cost variables: (i) staff (including medical, nursing and allied health salaries and wages), (ii) critical care, (iii) emergency department, (iv) diagnostic (including pathology, imaging, pharmacology and specialist procedure suites), (v) prosthesis, operating room, (vii) ward and (viii) other related costs (including hotel, non-clinical, on costs, patient transport). A detailed description of the cost variables can be found in Appendix 1.

Robotic system and maintenance cost

In December 2016, RPAH purchased Stryker's MAKO™ Robotic System, with the MAKO system software purchased in October 2018. The annualised cost of the MAKO™ system and software was calculated based on the total cost divided by ten years (estimated life span). The cost per case was calculated using the annualised cost divided by the number of cases performed during the respective period.

Stryker has a five year maintenance contract with RPAH. The annualised maintenance cost was obtained based on the total maintenance cost divided by five, and the annualised maintenance cost per patient was this number divided by the number of cases during the respective period. In addition to the abovementioned robotic costs, the total cost included the preoperative computerised tomography (CT) scan required to generate a 3D virtual model that is loaded into the MAKO System software, with the cost based on the corresponding Medicare Benefits Scheme allocated by the Australian Department of Health [19].

Computer-navigated system and maintenance cost

The Stryker ASM system annualised cost was calculated based on the total cost divided by ten years (expected life span). The cost per case was calculated using the annualised cost divided by the number of cases performed during the respective period. The annualised maintenance cost per patient was calculated by obtaining the total maintenance cost, dividing by the period of the study and then dividing by the number of cases performed during the respective period.

Statistical analysis

All statistical calculations were conducted using SPSS version 25. Categorical data is presented as frequencies (percentage), and continuous data is presented as mean and standard deviation (SD). These descriptive statistics were used to summarise patient characteristics, surgical outcomes and in-hospital cost. Patient characteristics and surgical outcomes between robotic-assisted and computer-navigated TKA were compared using independent Student's *t*-tests. The mean absolute difference between the cost variables was expressed with a mean difference (95% confidence intervals). A $p < 0.05$ was considered statistically significant for all performed analyses.

Results

During the study period, 385 TKAs were performed at RPAH. Of these, 127 were excluded due to the use of manual instrumentation ($n = 53$), other instrumentation ($n = 26$), bilateral TKAs ($n = 20$), limb-sparing mega-arthroplasty ($n = 15$) and revision cases ($n = 13$). Of the remaining 258 primary TKAs included in the study, 181 (70.2%) were computer navigated and 77 (29.8%) robotic assisted. The proportions of robotic-assisted and computer-navigated TKAs performed during the study period are presented in Fig. 1. Within 9 months of the study period, there was a linear increase in robotic-assisted TKAs and a linear decrease in computer-navigated TKA.

Patient characteristics

Overall, 60.5% of cases were female, the average age was 69.6 years and the vast majority had a diagnosis of knee osteoarthritis (96.5%). Patients undergoing computer-navigated TKA were slightly more likely to be female (64.6% vs 50.6%; $p = 0.035$), had a lower surgical time (82.9 min vs 113.4 min; $p < 0.001$) and total operating time (132.5 min vs 163.5 min; $p < 0.001$) and were less likely to be discharged home from an acute hospital (74.6% vs 88.3%; $p = 0.014$) with a longer overall length of stay including discharge from in-patient rehabilitation (8.8 days vs 6.8 days; $p = 0.013$) when compared to robotic-assisted TKA patients. Full demographic data is presented in Table 1.

Surgical system and maintenance cost

The upfront cost of robotic-assisted TKA included the cost of the MAKO Robotic System ($ 1,173,000), TKA MAKO software ($ 350,000), maintenance cost ($ 160,000 per year) and the preoperative CT scan for each patient ($ 220 per scan). Therefore, the annualised capital cost of each

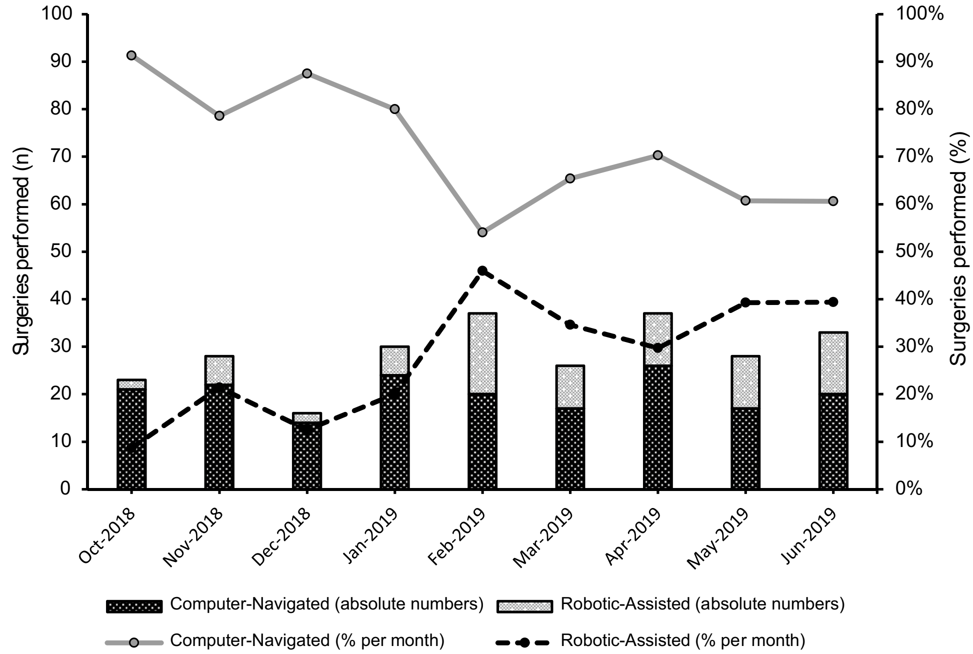

Fig. 1 Number of TKAs performed

robotic-assisted TKA was \$ 3160.5 per case, accounting approximately for 15% of the total robotic-assisted TKA cost.

The upfront cost of computer-navigated TKA included the cost of the ASM system combined with software (\$ 183,150) and maintenance cost (\$ 18,500 per year). Therefore, the annualised capital cost of computer-navigated TKA was \$ 147.5 per case, accounting approximately for 0.8% of the total navigation-assisted TKA cost.

In-hospital costs

Overall, there were statistically significant differences in costs over multiple categories (Table 2). The total cost, including capital costs of surgical equipment and maintenance costs, was less for the computer-navigated group compared to the robotic-assisted group (mean difference: \$ − 2359.1; 95% confidence intervals: \$ − 4359.1 to \$ − 656.2, $p=0.007$). The major difference was in the upfront capital costs of the robotic systems (\$ 147.5 in the computer-navigated group vs \$ 3160.5 in the robotic-assisted group). The computer-navigated group was also less expensive for operating room cost (mean difference: \$ − 734.1; 95% confidence intervals: \$ − 923.9 to \$ − 544.4, $p<0.001$) and other costs (mean difference: \$ − 276.5; 95% confidence intervals: \$ − 545.0 to \$ − 8.1, $p=0.044$). There was no significant difference between the two groups seen for staff, diagnostic, prosthesis, ward and overall acute in-patient cost. Appendix 2 shows the complete breakdown of the acute in-hospital cost analysis between these groups.

The robotic-assisted group was significantly less expensive for the average in-patient rehabilitation cost when spread within groups over the study period (\$ 1654.2 vs \$ 3652.0). This was due to the higher rate of inpatient rehabilitation required for the computer-navigated group ($n=46/181$, 25.4%) compared with the robotic-assisted group ($n=9/77$, 11.7%). There was no difference in the average cost for this sub-acute stay for those patients that did require it in each group (\$ 14,369.7 in the computer-navigated group vs \$ 14,152.7 in the robotic-assisted group; $p=0.925$).

Discussion

This study describes the detailed in-hospital cost of robotic-assisted TKA, along with the implementation cost accounting for upfront purchase of the robotic system and maintenance fees, compared to computer-navigated TKA in this Australian public healthcare system. The in-hospital cost of robotic-assisted TKA was equivalent to computer-navigated TKA and trended towards slightly cheaper when considering the higher discharge rate to home rather than in-patient rehabilitation. When the upfront surgical equipment and maintenance costs were added to the in-hospital cost, robotic-assisted TKA was significantly more expensive than computer-navigated TKA, though it should be noted that this is partly dependent on the relatively smaller number of cases performed with this technology during the study period and the per-case calculation method employed. This could be expected to reduce as the number of cases performed with

Table 1 Characteristics of patients undergoing computer-navigated and robotic-assisted total knee arthroplasty

RPAH Medical Centre, 100 Carillon Ave, Newtown NSW 2042 Characteristics	Computer-navigated TKA ($n=181$)	Robotic-assisted TKA ($n=77$)	*P* value
Age, years	70.2 ± 8.8	68.1 ± 10.3	0.096
Sex			0.035
Female	117 (64.6)	39 (50.6)	
Male	64 (35.4)	38 (49.4)	
Body mass index	33.1 ± 5.8	32.2 ± 5.8	0.239
ASA score			0.851
1	3 (1.7)	1 (1.3)	
2	86 (47.5)	34 (44.2)	
3	91 (50.3)	42 (54.5)	
4	1 (0.5)	0 (0)	
Country of birth			0.431
Australia	82 (45.3)	39 (50.6)	
Overseas	99 (54.7)	38 (49.4)	
Place of residence			0.094
Metropolitan area	169 (93.4)	67 (87.0)	
Remote area	12 (6.6)	10 (13.0)	
Health insurance			0.100
Public	136 (75.1)	65 (84.4)	
Private	45 (24.9)	12 (15.6)	
Diagnosis			0.611
Osteoarthritis	174 (96.1)	75 (97.4)	
Other diagnoses	7 (3.9)	2 (2.6)	
Surgical time, minutes	82.9 ± 17.0	113.4 ± 22.5	< 0.001
Operating time, minutes	132.5 ± 27.7	163.5 ± 27.2	< 0.001
Length of stay (acute), days†	5.2 ± 2.3	5.2 ± 2.0	0.947
Discharge destination			0.014
Home	135 (74.6)	68 (88.3)	
Another hospital/rehabilitation facility	46 (25.4)	9 (11.7)	
Length of stay (another hospital/rehabilitation facility), days (median ± IQR)	13.0 ± 7.3	12.0 ± 6.5	0.918
Total length of stay, days‡	8.8 ± 7.3	6.8 ± 5.2	0.013
Hospital re-admission within 28 days	0 (0)	0 (0)	–

Data presented as frequency (percentage) or mean ± standard deviation unless otherwise specified; *IQR*, interquartile range; *TKA*, total knee arthroplasty; *ASA*, American Society of Anesthesiologists physical classification system; Surgical time, time of knife to the skin to final stitch complete; Operating time, time commenced anaesthesia to the patient leaving the operating room. †Inclusive of the number of days for bed stay in the acute/primary hospital following the operation; ‡Patients who required ongoing bed stay at another hospital/rehabilitation facility; Other diagnoses included avascular necrosis ($n=3$; 1.2%), other inflammatory arthritis ($n=3$; 1.2%), rheumatoid arthritis ($n=1$; 0.4%), post-traumatic arthritis ($n=1$; 0.4%), and haemophilia leading to degenerative arthritis ($n=1$; 0.4%)

this technology increases, as is predicted by the trend of the technology uptake curves (Fig. 1). The cost of the implant remains the main cost driver for both robotic-assisted and computer-navigated TKA total costs. The cost of the disposable equipment did not differ between the two surgical approaches. The robotic system purchase and maintenance costs accounted for approximately 15% of the robotic-assisted TKA total cost, but only 0.8% of the navigated TKA cost when analysed in this study. Surgical time and operating time were both significantly longer in robotic-assisted TKA; robotic-assisted TKA cases were more likely to be discharged directly home and have an overall shorter length of stay, when compared to computer-navigated TKA, with a corresponding cost-saving.

To the author's knowledge, this is one of the first studies to provide a detailed in-hospital cost breakdown of robotic-assisted TKA, compared to computer-navigated TKA. Despite significant differences in surgical and operating time, no difference was found within the total in-hospital costs when comparing robotic-assisted and

Table 2 Cost comparison between computer-navigated and robotic-assisted total knee arthroplasties

Cost variables	Computer navigated ($n=181$)	Robotic assisted ($n=77$)	Mean difference (95% confidence intervals)	P value
Staff	3267.0 ± 1137.0	3205.4 ± 827.3	61.6 (− 188.2 to 311.3)	0.627
Diagnostic	228.5 ± 152.0	231.6 ± 123.6	− 3.1 (− 41.7 to 35.6)	0.876
Prostheses	5803.6 ± 641.3	5693.7 ± 747.2	109.9 (− 83.2 to 303.0)	0.262
Operating room	2,810.9 ± 572.2	3545.0 ± 753.2	− 734.1 (− 923.9 to − 544.4)	< 0.001
Ward	491.5 ± 236.3	481.8 ± 188.6	9.7 (− 50.1 to 69.5)	0.750
Other costs	3258.8 ± 931.1	3535.4 ± 1152.7	− 276.5 (− 545.0 to − 8.1)	0.044
Patients requiring sub-acute stay at another hospital/rehabilitation facility‡	14,369.7 ± 6,577.5 ($n=46$; 3652.0 per patient)	14,152.7 ± 4350.7 ($n=9$; 1654.2 per patient)	217.0 (− 4382.9 to 4816.9)	0.925
Total cost (excluding surgical equipment and maintenance cost)	19,512.3 ± 7,698.6	18,347.1 ± 5672.9	1165.2 (− 537.7 to 2868.1)	0.179
Capital cost of surgical equipment and maintenance cost per patient	147.5 ± 0	3160.5 ± 0	− 3013.0 (0 to 0)	
Total cost (including surgical equipment and maintenance cost)	19,659.7 ± 7698.6	21,507.6 ± 5672.9	− 1847.9 (− 3550.8 to − 145.0)	0.034

Data presented as mean ± standard deviation, unless otherwise indicated; Mean difference, negative value favours computer-navigated cohort; ‡Patients who required ongoing bed stay at another hospital/rehabilitation facility ($n=55$), with the number of patients contributing to calculation and distributed cost of sub-acute stay per patient within the group over the study period in brackets. Detailed cost details can be found in Appendix 1

computer-navigated TKA ($ 18,347.1 vs $ 19,512.3). The additional upfront cost of the robotic system and maintenance fees resulted in a total cost mean difference of $ 2,359.1 favouring computer-navigated TKAs. Similar results have been reported by Moschetti and Colleagues, when investigating the cost-effectiveness of robotic UKA [16]. The total cost including the robotic system, preoperative CT scan, robotic maintenance fees and in-hospital care was US$ 19,219 compared to US$ 16,476 from conventional UKA. In fact, robotic-assisted UKA was only found to be cost-effective when a larger amount of cases were performed (>94 per year), they presented a low failure rate (<1.2% at 2 years), had an improved failure rate after two years, the cost of the robotic system and maintenance was <US$ 1.4 million, the robotic system lifespan was ≥4.7 years and the patients were younger (<67 years). Therefore, the detailed cost of robotic-assisted TKA is extremely valuable for centres that are planning to implement a robotic system within their hospitals. In the current study, we observed a linear increase in the number of robotic-assisted TKAs. Should this trend be maintained, the cost of robotic-assisted TKA would equate to computer-navigated within 23 months from its implementation. To the same extent, increasing the number of robotic-assisted TKAs to 238 procedures per year would also demonstrate an equivalence in cost.

In a study conducted by Cool and Colleagues, the cost of a 90-day episode of care was compared between robotic-assisted TKA ($n=519$) and conventional TKA ($n=2595$). Interestingly, at 90-day post-operatively, the cost of an episode of care was significantly less for robotic-assisted TKA (US$ 18,568 vs US$ 20,960). Some of the contributors to the lower 90-day episode cost for the robotic-assisted TKA cases were shorter length of hospital stay (4.07 days vs 4.14 days), higher likelihood to be discharged home (84.2% vs 70.3%) and lower re-admission rate (5.2% vs 7.8%). The current study demonstrated similar findings in regards to the admission rate to rehabilitation and overall hospital stay. While no difference in length of acute hospital stay (5.2 days vs 5.2 days) or hospital re-admission within 28 days (0% vs 0%) was seen, robotic-assisted TKA patients were more likely to have a shorter length of overall stay once patients requiring a sub-acute in-patient stay in rehabilitation were considered (6.8 days vs 8.8 days) as discharge directly to home was significantly higher in the robotic-assisted group (88.3% vs 74.6%). This study did show a longer surgical (113.4 min vs 82.9 min) and operation time (163.5 min vs 132.5 min) for robotic-assisted surgery. While this finding may have been influenced by the introduction of the robot to the facility and consequent selection of patients based on robotic surgical proficiency, it is unlikely this would substantially alter these findings.

As this study described the upfront costs and in-hospital costs between robotic-assisted and computer-navigated TKA, including the implementation phase of the robotic-assisted system at our facility, these results may not be relevant to other facilities that have similar programmes running for longer periods. In addition, the in-hospital costs may be hospital specific, due to the fact that each hospital and system has different contracts and arrangements for their equipment. Therefore, it is important that further research within different centres perform a similar analysis to confirm the presented results. Furthermore, as this study describes the in-hospital cost on the first 77 robotic-assisted TKA performed in a tertiary hospital, the surgeons and theatre team learning curve may have affected the cost of robotic-assisted TKA and the surgical and operating time. However, there are reports in the literature that corroborate our findings, where robotic-assisted TKA was associated with significantly longer operation time [20]. This was mainly attributed to the time taken to set up the robotic system in theatres. Recently, Kayani and colleagues reported that the implementation of robotic-assisted TKA increased operative times and that the learning curve among the surgical team was overcome within the initial seven robotic-assisted TKA cases [21]. The potential association between surgical and operating time on the length of stay, and thus total in-hospital costs, requires further exploration. Lastly, longer term data on TKA survivorship following RAS is essential when considering cost-effectiveness in this population, as a decrease in revision rates and improvement of function and pain outcomes would easily equipoise the initial cost of the new technology.

The introduction of new technology in surgery is commonly associated with an initial increase in cost [14]. This is generally due to the upfront cost of the technology, software, instruments and surgical team learning curve. However, given the evolution of new technology and innovation over time, consideration of costs should be undertaken in a broader context rather than in isolation. Thus, future studies are required to demonstrate the clinical benefit of robotic-assisted TKA while considering the upfront cost of the system and to explore the costs across competing robotic systems.

Conclusions

This study provides an in-depth description of in-hospital costs of robotic-assisted and computer-navigated primary TKA. No difference in the in-hospital total cost was observed between robotic-assisted and computer-navigated TKA. When the upfront cost of the surgical equipment, including MAKO robot, pre-operative CT scan, software and maintenance fees were added to the in-hospital cost, robotic-assisted TKA was significantly more expensive than computer-navigated TKA. Surgical and operating times were longer in robotic-assisted TKA cases; however, patients were more likely to be discharged home without the need for inpatient rehabilitation.

The implementation of new technology often comes with an associated initial cost, and longer term cost analysis of robotic-assisted TKA should be investigated in future studies. As the technology gains increased utilisation over time, the per-case cost tends to fall, and in this series, this would be projected to occur approximately 23 months after the implementation of the robotics programme based on observed trends.

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Author contributions All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by Daniel Steffens, Sascha Karunaratne, Kate McBride, Sanjeev Gupta, Mark Horsley and Brett Fritsch. The first draft of the manuscript was written by Daniel Steffens and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Data availability Data are available upon reasonable request.

Code availability Not applicable.

Declarations

Additional declarations for articles in life science journals that report the results of studies involving humans and/or animals Not applicable.

Ethics approval Ethics approval was granted by the Sydney Local Health District Human Ethics Committee (X19-0456, HREC number: 2019/ETH13554).

Consent to participate Waiver of consent granted by the Sydney Local Health District Human Ethics Committee.

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Competing interests The authors declare no competing interests.

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