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Practicality of Conducting a Randomized Controlled Trial to Identify Differences in Revision Risk Between Conventional and Technology-Assisted Total Knee Arthroplasty Procedures in a Patient Population at Elevated Risk of Revision – A Simulation Study

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Abstract

Given evidence that patients with a lower age at index surgery and higher BMI have an enhanced risk of aseptic revision. In this study we used a previously developed methodology to estimate how large a comparative study would need to be to detect differences between navigated/robotic TKA and conventional TKA in both higher- and lower-risk patient populations, and how long the follow-up periods would need to be to be sufficiently powered to detect those differences.

We modeled and simulated the likely outcomes of potential RCT study designs according to our previously published method. We generated three large sets of patients with distributions of patient-specific factors characteristic of patients at a reduced or enhanced risk of aseptic revision (relative to the typical risk assumed in our previous study). We then computed the corresponding Kaplan-Meier survival curves and applied a log-rank test to each study for statistical differences in revision rates at concurrent follow-up timepoints.

The results from our simulation found survivorship differences favoring TA-TKA ranging from 2.8% to 3.9% at 15- and 20-years follow-up on the patient population at an enhanced risk of aseptic revision. Even for the patient population at the highest baseline risk of aseptic revision, comparative studies would still need to enroll at least 1750

patients in each arm of the study to have an 80% chance of showing this reduction in revision rates at 15 years of follow-up. Traditional RCT studies would require impractically large numbers of patients to be enrolled and excessively long follow-up times to demonstrate whether such a reduction actually exists.

1 Introduction

Technology-assisted total knee arthroplasty (TA-TKA) procedures – using navigated or robot-assisted systems – have been introduced with the goal of improving implant survival and other clinical outcome measures through enhanced precision and accuracy of bone resections and placement of components [1 - 4]. However, no sufficiently powered randomized controlled trial (RCT) has shown that such interventions result in improved implant survival [2 - 9]. This is not surprising given that, in a previous simulation study, we showed that RCTs would need to enroll an impractically high number of patients – between 2500 and 4000 patients in each arm of the study, depending on the precision of the TA-TKA procedure – to have an 80% chance of showing a reduction in revision rate ranging between 1.4% - 2.0% at 15 years of follow-up. However, the previous study considered a patient population with demographic characteristics (such as age at index surgery, body mass index (BMI), and sex) that put the patients at a mid-range overall risk of revision. Given evidence that patients with a lower age at index surgery and higher BMI have an enhanced risk of aseptic revision [10], [11], [12], in this study we used the same simulation methodology to estimate how large a comparative study would need to be to detect differences between TA-TKA and conventional TKA in both higher- and lower-risk patient populations, and how long the follow-up periods would need to be to be sufficiently powered to detect those differences.

2 Methods

Using estimated effect sizes drawn from previous clinical and registry studies, combined with estimates of the accuracy and precision of TA-TKA, we modeled and simulated the likely outcomes of potential RCT study designs according to our previously published method [13]. Using this method, we generated three large sets of patients with distributions of patient-specific factors characteristic of patients at a reduced or enhanced risk of aseptic revision (relative to the typical risk assumed in our previous study). Each population was characterized by a characteristic survival time (τ), which parameterizes a bi-exponential survival function representing the combined influence of various patient-specific risk factors on the baseline revision rate of that simulated patient population. More plainly, τ defines the drop-off of the survival curve, with a lower number resulting in lower probability of implant survival. We selected three different values of τ to characterize three different patient populations with differing levels of revision risk: a medium-risk population matching that reported in our initial simulation-based study (mean age at index surgery: 67 years, mean BMI: 27 kg/m2, τ = 75 years), and both lower- and higher-risk populations (mean age at index surgery: 77 years, mean BMI: 23 kg/m2, τ = 80 years, and mean age at index surgery: 56 years, mean BMI: 34 kg/m2, τ = 60 years, respectively).

We then simulated the revision outcomes for these three risk categories of simulated patient populations under two different surgical techniques with different precisions: conventional (coronal alignment standard deviation $\sigma = 2.95^{o}$) and enhanced precision ($\sigma = 1.0^{o}$ – at the lower limit of reported variability for TA-TKA systems). To evaluate the power associated with using different cohort sizes, we first generated a random set of 1.5 million simulated patients for each risk class and then ran a Monte Carlo simulation generating 1000 simulated populations of various cohort sizes by drawing the requisite

number of patient samples (with replacement) from each of the large sets of simulated patients from each risk class. We simulated the time to revision for aseptic loosening for each patient under the two different surgical precisions, computed the corresponding Kaplan-Meier survival curves, and applied a log-rank test to each study for statistical differences in revision rates at concurrent follow-up timepoints (1-25 years). From each simulation associated with a given cohort size, we determined the percentage of simulated studies that found a statistically significant difference at each follow-up interval. We then calculated the expected reduction in revision rates attributable to TA-TKA for the entire set of Kaplan-Meier survival analyses.

3 Results

The results from our simulation found survivorship differences favoring TA-TKA (compared with conventional surgery) ranging from 2.8% to 3.9% at 15- and 20-years follow-up (relative to baseline implant survival rates of 89.5% and 82.9%) on the patient population at an enhanced risk of aseptic revision (Figure 1). Even for the patient population at the highest baseline risk of aseptic revision, comparative studies would still need to enroll at least 1750 patients in each arm of the study (3500 total) to have an 80% chance of showing this reduction in revision rates at 15 years of follow-up (Figure 2), compared with approximately 2300 in each arm (4600 total) in the average-risk population previously reported. The lower-risk population would require closer to 2700 patients in each arm (5400 total).

4 Discussion

Based on these simulations, TA-TKA interventions with enhanced precision are estimated to reduce revision rates in TKA (by ~2.8% at 15 years, compared to our baseline simulation showing 2.0%, which would be excellent for affected patients). However, the reduction in revision rates is still relatively small in comparison with the baseline success rate of TKA and would not reach this level of difference until 15 years after the index surgery. Performing an RCT in an enhanced risk population would still require an impractically large number of patients in each arm (1750 vs 2300, for the mid-range risk category, or only about a 25% reduction in RCT size) to be properly powered.

This study has several important limitations. First, we inferred the effects of patient-specific and surgeon-controlled factors on the implant revision rates but did not directly measure or verify such effects. One of which is that our risk models are based on risk data acquired from large clinical studies, systematic reviews, and registry studies, and capture what we believe are reasonable estimates of the effect size of TA-TKA on revision rates. A comprehensive list of limitations can be found in our original simulation publications [12], [13].

5 Conclusion

Even when focused on patient populations at relatively higher risk of aseptic revision, traditional RCT studies would require impractically large numbers of patients to be enrolled and excessively long follow-up times to demonstrate whether such a reduction actually exists. Therefore, in agreement with the conclusions of our previous study, we recommend that researchers cease trying to demonstrate reductions in revision risk between TA-TKA and conventional surgical approaches using a comparative study approach where TA-TKA is applied to a broad patient population, even when the demographics of the population put its members at enhanced risk of revision, as the estimated effect size is too small to be detected with reasonable numbers of patients in a reasonable period of follow-up. Instead, we

recommend they focus on evaluating other potential benefits of TA-TKA, such as improvements to patient-reported and functional outcome measures.

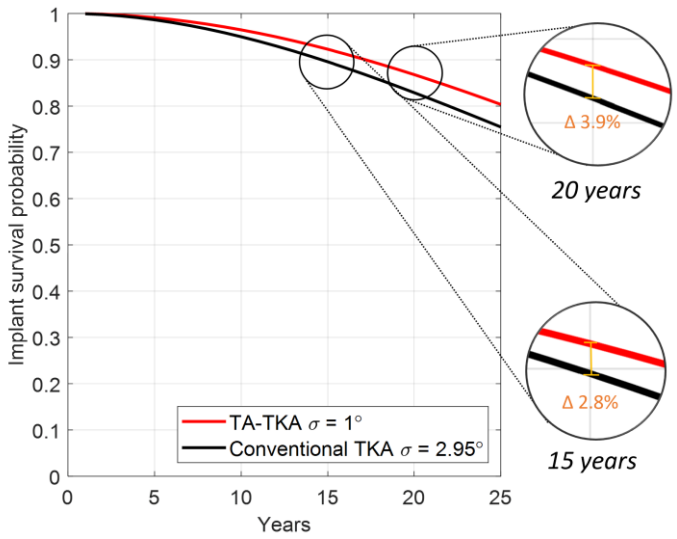

Figure 1: Kaplan-Meier survival curves for conventional TKA (black) and technology-assisted (TA) TKA in a higher-risk patient population. Bubbles show the estimated reduction in revision rates attributable to TA-TKA intervention at 15- and 20-years post index.

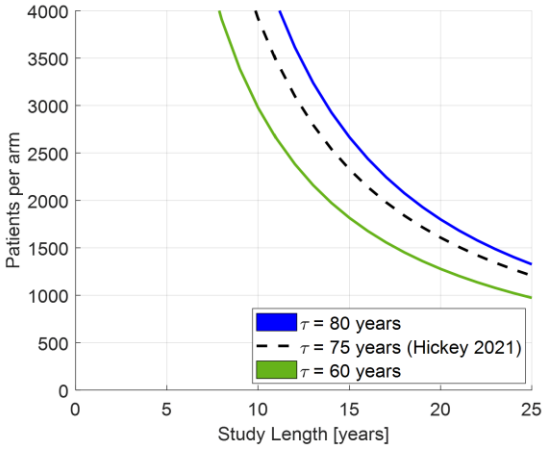

Figure 2: Curves showing the study design (mean follow-up time and number of enrolled patients in each arm of the study) for a survival analysis to have an 80% probability of rejecting the null hypothesis ($p < 0.05$) on various populations with either an enhanced (green) or reduced (blue) risk of aseptic revision. The black dotted line indicates the patient population simulated in our original study [13]. This simulation was done assuming an effect size (that is, difference in the revision rate) for a coronal alignment precision of $\sigma = 1.0°$. The precision of the conventional group was assumed to be $\sigma = 2.95°$.

References

[1] B. Kayani, S. Konan, A. Ayuob, E. Onochie, T. Al-Jabri, and F. S. Haddad, "Robotic technology in total knee arthroplasty: A systematic review," *EFORT Open Rev*, vol. 4, no. 10, pp. 611–617, 2019, doi: 10.1302/2058-5241.4.190022.

[2] D. Hernández-Vaquero, A. Suarez-Vazquez, and S. Iglesias-Fernandez, "Can computer assistance improve the clinical and functional scores in total knee arthroplasty?," *Clin Orthop Relat Res*, vol. 469, no. 12, pp. 3436–3442, 2011, doi: 10.1007/s11999-011-2044-2.

[3] M. Ollivier, S. Parratte, L. Lino, X. Flecher, S. Pesenti, and J. N. Argenson, "No benefit of computer-assisted TKA: 10-year results of a prospective randomized study," *Clin Orthop Relat Res*, vol. 476, no. 1, pp. 126–134, Jan. 2018, doi: 10.1007/s11999.0000000000000021.

[4] H. Y. Yang, J. K. Seon, and Y. J. Shin, "Robotic Total Knee Arthroplasty with a Cruciate-Retaining Implant: A 10-Year Follow-up Study," pp. 169–176, 2017, doi: 10.4055/cios.2017.9.2.169.

[5] Y. H. Kim, J. W. Park, and J. S. Kim, "2017 Chitranjan S. Ranawat Award: Does Computer Navigation in Knee Arthroplasty Improve Functional Outcomes in Young Patients? A Randomized Study," in *Clinical Orthopaedics and Related Research*, Lippincott Williams and Wilkins, Jan. 2018, pp. 6–15. doi: 10.1007/s11999.0000000000000000.

[6] Y. H. Kim, J. W. Park, and J. S. Kim, "The clinical outcome of computer-navigated compared with conventional knee arthroplasty in the same patients: A prospective, randomized, double-blind, long-term study," *Journal of Bone and Joint Surgery - American Volume*, vol. 99, no. 12. Lippincott Williams and Wilkins, pp. 989–996, 2017. doi: 10.2106/JBJS.16.00791.

[7] K. J. Cho, J. K. Seon, W. Y. Jang, C. G. Park, and E. K. Song, "Robotic versus conventional primary total knee arthroplasty: clinical and radiological long-term results with a minimum follow-up of ten years," *Int Orthop*, vol. 43, no. 6, pp. 1345–1354, Jun. 2019, doi: 10.1007/s00264-018-4231-1.

[8] J. Cip, F. Obwegeser, T. Benesch, C. Bach, P. Ruckenstuhl, and A. Martin, "Twelve-Year Follow-Up of Navigated Computer-Assisted Versus Conventional Total Knee Arthroplasty: A Prospective Randomized Comparative Trial," *Journal of Arthroplasty*, vol. 33, no. 5, pp. 1404–1411, May 2018, doi: 10.1016/j.arth.2017.12.012.

[9] J. Cip, M. Widemschek, M. Luegmair, M. B. Sheinkop, T. Benesch, and A. Martin, "Conventional versus computer-assisted technique for total knee arthroplasty: A minimum of 5-year follow-up of 200 patients in a prospective randomized comparative trial," *Journal of Arthroplasty*, vol. 29, no. 9, pp. 1795–1802, 2014, doi: 10.1016/j.arth.2014.04.037.

[10] L. E. Bayliss *et al.*, "The effect of patient age at intervention on risk of implant revision after total replacement of the hip or knee: a population-based cohort study," *The Lancet*, vol. 389, no. 10077, pp. 1424–1430, Apr. 2017, doi: 10.1016/S0140-6736(17)30059-4.

[11] L. Boyce *et al.*, "The outcomes of total knee arthroplasty in morbidly obese patients: a systematic review of the literature," *Archives of Orthopaedic and Trauma Surgery*, vol. 139, no. 4. Springer Verlag, pp. 553–560, Apr. 01, 2019. doi: 10.1007/s00402-019-03127-5.

[12] M. D. Hickey, B. A. Masri, and A. J. Hodgson, "Can technology assistance be cost effective in TKA? A simulation-based analysis of a risk-prioritized, practice-specific framework," *Clin Orthop Relat Res*, vol. 481, no. 1, pp. 157–173, Jan. 2023, doi: 10.1097/CORR.0000000000002375.

[13] M. D. Hickey, C. Anglin, B. Masri, and A. J. Hodgson, "How large a study is needed to detect TKA revision rate reductions attributable to robotic or navigated technologies? A simulation-based power analysis," *Clin Orthop Relat Res*, vol. 479, no. 11, pp. 2350–2361, Nov. 2021, doi: 10.1097/CORR.0000000000001909.