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Cost utility modeling of early vs late total knee replacement in osteoarthritis patients

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SUMMARY

Given the dramatic increase in the number of total knee replacement (TKR) surgeries in developed countries, the issue of the best time for surgery needs to be addressed from an economic perspective.
Objective: To assess, from the perspective of the healthcare payer, the cost-utility of two surgical strategies in which knee replacement is performed at the early or late stage of the disease in patients with knee osteoarthritis (OA).
Design: Patient data and evidence from published literature on economic costs and outcomes in OA, including utilities, non-pharmacological, pharmacological and surgical options, combined with population life tables were entered in a Markov model of OA. The model represented the lifetime experience of a cohort of patients following their therapeutic management, discounting costs (euros) and utilities (quality-adjusted life-years) at 4% annually.
Results: In the base-case scenario, early TKR cost €6,624 more than late TKR (€76,223 vs €69,599) with a 0.15 gain in QALYs (18.675 vs 18.524). This yielded an incremental cost-utility ratio (ICUR) of 43,631 €/QALY. Sensitivity analyses of the most influential uncertain parameters were performed and did not modify the direction of the conclusions: early TKR cost between €3,655 and €7,194 more than late TKR with a gain in QALYs between 0.15 and 0.39. The ICUR ranged from 17,131 €/QALY to 48,241 €/QALY.
Conclusion: Our data do not support the early TKR strategy over the late TKR strategy in knee OA patients from a medico-economic perspective.

Introduction

Osteoarthritis (OA) is the most common type of arthritis and one of the leading causes of global disability. Indeed, OA was estimated to be the tenth leading cause of non-fatal burden in the world in 1990[1] and the eleventh highest contributor to global disability in 2010[2].

International guidelines recommend a combination of non-pharmacological and pharmacological[3,4] treatments to alleviate pain and improve function in knee OA patients. In those patients poorly controlled with this approach, knee replacement is recommended[3]. In spite of these recommendations and the fact that knee replacements have a limited lifespan, we lack a clear consensus to decide the best time for knee surgery. In real-life, indication for surgery varies greatly among countries, depending on habits of the physicians (doctor's and/or surgeon's opinion), the health-care system and the severity of the disease[5]. The development of a composite index that could inform on the severity of OA and which could help the decision to implement surgery has been pursued by an OARSI/OMERACT initiative[5]. However, no cutpoint for pain and for physical disability has yet been found that accurately discriminates the recommendation for total knee replacement (TKR). De facto, some knee OA patients have a TKR at an early stage of the disease whereas others have a late recourse to surgery options preceded by a prolonged non-pharmacological and pharmacological management. A survey[6] found that in France 22.8% of TKR were performed on patients younger than 65 whereas in Germany it was 26.7%.

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In addition, in some countries such as Canada and UK, there are waiting lists for TKR that may result in delayed surgery for suffering patients who were considered as eligible[7]. By contrast, in other countries such as France, Norway, Netherlands, accessibility to TKR is easier mostly due to universal coverage of health system and surgeons' availability. Although TKR has been shown to be cost-effective[8], the best strategy regarding early vs late TKR from a cost and utility perspective has never been assessed. While the best level of evidence for demonstrating the superiority of one strategy over another (early vs late TKR) would be obtained through randomized clinical trials (RCTs) comparing both utility and costs of alternatives, it is impossible to run such a study when practices are already in operation (with a specific – or not – selection of patients for each indication). Therefore a modeling approach is a useful tool to reflect elements of strategies, be it implemented now or in the future.

In this study, we aimed to investigate the cost and cost-utility of two different strategies for managing patients with knee OA: (1) late surgical management strategy ("late TKR") vs (2) early surgical management strategy ("early TKR").

Method

Model design

A Markov, state-transition, computer-based simulation model was developed to describe the course of a hypothetical cohort of patients with knee OA. The state-transition Markov model characterizes the course of a specific condition in an individual patient as a sequence of transitions from one state to another according to probabilities of each transition.

We used this model to examine the incremental cost-utility of two therapeutic management strategies of knee OA: (1) a therapeutic management with a preference for non-pharmacological and pharmacological options of knee OA and surgical option (as last resource – "late TKR"); (2) an earlier surgical management ("early TKR").

Base-case scenario

The full model consists of five major states (Fig. 1 and Supplementary Materials): (1) non-pharmacological treatment (NPh) option; (2) both non-pharmacological and pharmacological treatments (NPPh) option; (3) pharmacological treatment (Ph) option; (4) surgical treatment (Surg) option; and (5) death. For the first four states, the specifications followed international guidelines on OA management[3,5] and were as follows. For the NPh option: (1.1) aids (insoles, wedges, *etc.*); (1.2) physiotherapy (PT); and (1.3) others (education, weight loss, exercise, *etc.*). For the NPPh option: (2.1) aids and acetaminophen; (2.2) aids and nonsteroidal anti-inflammatory drugs (NSAIDs); (2.3) aids and symptomatic slow acting drugs for OA (SYSADOAs); (2.4) PT and acetaminophen; (2.5) PT and NSAIDs; (2.6) PT and SYSADOAs; and (2.7) other combination. For the Ph option: (3.1) acetaminophen; (3.2) NSAIDs; (3.3) SYSADOAs; (3.4) acetaminophen and NSAIDs; (3.5) acetaminophen and SYSADOAs; (3.6) SYSADOAs and NSAIDs; (3.7) corticosteroid injections; (3.8) HA injections; and (3.9) opioids. For the Surg option, (4.1) non prosthetic surgery (arthroscopy or osteotomy) and (4.2) replacement surgery [(unicompartimental knee replacement – UKR – or TKR)] were considered (See Fig. 1).

A healthcare payer perspective was taken, and only direct medical costs as reimbursed by the French National Health System (NHS) were taken into account. The cohort composition was defined by age to mirror the French population distribution (40–75 years) of OA patients[9].

Transitions occurred for 30 years, at which point remaining cohort survivors were assumed to die. Conditional on the initial age and Markov state, the model represented a series of contingent transitions until death: after each evaluation cycle (set at 3 months, i.e., the usual average time between two medical consultations in France for patients with OA), patients could either transition to another state or remain in the same state for another cycle with probability depending on their current state and improved health. Patients could transition from any state to the absorbing death state, based on age specific mortality rates obtained from French national life tables[10], and excess mortality associated with perioperative and drug-related mortalities.

In each cycle, the patient incurred costs and accrued utilities according to the state occupied. Utilities were measured as quality-adjusted life-years (QALYs): each cycle was assigned a utility payoff, i.e., a preference-based valuation of health-related quality of life (EQ-5D) in the occupied Markov state, on a scale ranging from zero (states equivalent to death), to one (representing full health).

As a result, total utilities and costs were the sum of QALYs and the sum of costs over the modeled lifespan of the cohort and were reported on a present-value basis using a 4% annual discount rate, as per French Health authorities' guidelines[11].

Incremental cost-utility ratio (ICUR) was assessed in the model by comparing the "early TKR" strategy with the "late TKR" strategy: ICUR was calculated as the difference in costs between both strategies divided by the difference in utility: (Cost "early TKR" – Cost "late TKR")/(Utility "early TKR" – Utility "late TKR"). The resulting ICUR expressed the comparative cost in euros per QALY gained.

Sensitivity analyses

We evaluated the stability of findings to variations in the values of input parameters using deterministic sensitivity analyses. All parameters were considered and only the sensitivity analyses with a conservative approach were presented. Indeed, we wanted to see how robust the model and the conclusions were even when both strategies were varied to render the choice as indifferent as possible.

The model was developed and implemented using TreeAge Pro software (TreeAge Pro Suite 2015, version 1.0, Williamstown, Massachusetts).

Literature search

A literature search was performed to retrieve data on outcomes and Western Ontario and McMaster Universities (WOMAC) scores.

For outcomes and WOMAC scores, the systematic literature review undertaken for the OARSI recommendations was used[3]. Data from studies that showed WOMAC scores and variations in WOMAC pain scores were retrieved.

Two recent French studies presenting an evaluation of health resources utilized in managing OA were used to complete the search on resources and costs retrieved from French public databases[12,13].

Costs

Only direct costs from the perspective of the French NHS were investigated. These costs included medical consultations, prescriptions costs over the cycle length and hospitalization (UKR, TKR) costs. Gastrointestinal (GI), cardiovascular (CV) and renal adverse events (AE) associated to NSAIDs and opioids were also taken into consideration and were valued based on their probability of occurrence in knee OA patients[14]. The costs of inpatient rehabilitation following arthroplasty were included. See Supplementary Materials for the description of AEs and inpatient rehabilitation.