Analyzing cost-effectiveness of ulnar and median nerve transfers to regain forearm flexion

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OBJECTIVE Peripheral nerve transfers to regain elbow flexion via the ulnar nerve (Oberlin nerve transfer) and median nerves are surgical options that benefit patients. Prior studies have assessed the comparative effectiveness of ulnar and median nerve transfers for upper trunk brachial plexus injury, yet no study has examined the cost-effectiveness of this surgery to improve quality-adjusted life years (QALYs). The authors present a cost-effectiveness model of the Oberlin nerve transfer and median nerve transfer to restore elbow flexion in the adult population with upper brachial plexus injury.

METHODS Using a Markov model, the authors simulated ulnar and median nerve transfers and conservative measures in terms of neurological recovery and improvements in quality of life (QOL) for patients with upper brachial plexus injury. Transition probabilities were collected from previous studies that assessed the surgical efficacy of ulnar and median nerve transfers, complication rates associated with comparable surgical interventions, and the natural history of conservative measures. Incremental cost-effectiveness ratios (ICERs), defined as cost in dollars per QALY, were calculated. Incremental cost-effectiveness ratios less than $50,000/QALY were considered cost-effective. One-way and 2-way sensitivity analyses were used to assess parameter uncertainty. Probabilistic sampling was used to assess ranges of outcomes across 100,000 trials.

RESULTS The authors’ base-case model demonstrated that ulnar and median nerve transfers, with an estimated cost of $5066.19, improved effectiveness by 0.79 QALY over a lifetime compared with conservative management. Without modeling the indirect cost due to loss of income over lifetime associated with elbow function loss, surgical treatment had an ICER of $6453.41/QALY gained. Factoring in the loss of income as indirect cost, surgical treatment had an ICER of $96,755.42/QALY gained, demonstrating an overall lifetime cost savings due to increased probability of returning to work. One-way sensitivity analysis demonstrated that the model was most sensitive to assumptions about cost of surgery, probability of good surgical outcome, and spontaneous recovery of neurological function with conservative treatment. Two-way sensitivity analysis demonstrated that surgical intervention was cost-effective with an ICER of $18,828.06/QALY even with the authors’ most conservative parameters with surgical costs at $50,000 and probability of success of 50% when considering the potential income recovered through returning to work. Probabilistic sampling demonstrated that surgical intervention was cost-effective in 76% of cases at a willingness-to-pay threshold of $50,000/QALY gained.

CONCLUSIONS The authors’ model demonstrates that ulnar and median nerve transfers for upper brachial plexus injury improves QALY in a cost-effective manner.

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KEY WORDS cost-effectiveness; nerve transfer; peripheral nerve surgery; upper brachial plexus injury; nerve transfer surgery; Oberlin procedure; median nerve transfer

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ABBREVIATIONS CPT = Current Procedural Terminology; EMG = electromyography; ICER = incremental cost-effectiveness ratio; MRC = Medical Research Council; QALY = quality-adjusted life year; QOL = quality of life; WTP = willingness-to-pay.

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ment and operative management. Compared with conservative measures, surgical intervention via nerve transfers has been shown to significantly improve neurological function.\textsuperscript{15,18,27}

Prompt surgical intervention within 6 months of injury has been associated with a more favorable outcome compared with delayed surgical treatment.\textsuperscript{4} For patients who undergo conservative treatment, 12\%–41\% may experience spontaneous recovery within the first 3 months.\textsuperscript{15,18} However, after this interval, spontaneous recovery and restoration of full neurological function becomes increasingly less likely. While multiple nerve transfers may be indicated to address additional deficits that result from an upper brachial plexus injury,\textsuperscript{26} restoration of elbow flexion remains the highest priority.\textsuperscript{3} Various nerve transfer approaches are available for restoring elbow flexion with remarkable rates of success\textsuperscript{3,7} and minimal reduction in functionality of the donor nerve.\textsuperscript{6} The Oberlin procedure,\textsuperscript{23} established in 1994, utilizes transfer of a fascicle of the ulnar nerve to the biceps branch of the musculocutaneous nerve to regain forearm flexion at the elbow. Similarly, a fascicle of the median nerve transferred to the biceps branch of the musculocutaneous nerve is also effective in improving elbow flexion.\textsuperscript{1,8,19} A double fascicular transfer that uses both ulnar and median nerve fascicles to reinnervate musculocutaneous branches to both biceps and brachialis muscles has been argued to provide additional strength.\textsuperscript{16} Although prior studies have investigated the comparative efficacy of these nerve transfer procedures,\textsuperscript{3} a cost-effectiveness study of surgical management compared with conservative management has not yet been conducted.

To our knowledge, we present the first cost-effectiveness model to demonstrate the incremental cost-effectiveness ratio (ICER) for ulnar and median nerve transfers in patients with upper brachial plexus injury. We aim to not only show cost-effectiveness of nerve transfer surgery on an individual and societal level, but also to highlight this underutilized time-sensitive surgical strategy and encourage early referral of potential surgical candidates by medical decision makers.

**Methods**

**Treatment Strategies**

Our decision model captures the choice between surgical and nonsurgical management 4.5 months after initial upper brachial plexus injury. We chose 4.5 months to capture the patient population with persistent neurological deficit with unlikely spontaneous recovery (Fig. 1).\textsuperscript{15,18} The competing treatment strategies in our models were as follows: Strategy 1, nonsurgical management of upper brachial plexus injury with a small chance of spontaneous neurological recovery; and Strategy 2, surgical management of upper brachial plexus injury via ulnar nerve transfer, median nerve transfer, or the combination of both branches of the ulnar and median nerves to reinnervate motor branches of the biceps to restore elbow flexion.

**Decision Model**

A decision-analysis model was constructed to assess the cost-effectiveness of ulnar and median nerve transfers in patients with loss of elbow flexion secondary to upper brachial plexus injury 4.5 months after injury. The role of additional nerve transfers to restore shoulder function was not included in this model. This model used carefully selected data from our literature review that included studies on health-related QOL and quality-adjusted life years (QALYs). The base scenario involved a 28-year-old male patient, with 50 years of life expectancy,\textsuperscript{8} with loss of C-5 and C-6 function without spontaneous recovery 4.5 months after injury. Using a Markov model, each “patient” underwent 50 cycles (1 year per cycle) to model the lifetime QOL impact of each functional state. The decision-analysis model is illustrated in Fig. 2.

**Outcomes**

Elbow flexion, categorized by the British Medical Research Council (MRC) score to assess neurological strength, was chosen as the primary clinical outcome.\textsuperscript{3,24,27} The 3 categories for surgical outcome were good, fair, and poor, each corresponding to MRC grades of 4–5, 2–3, and
Cost-effectiveness of ulnar and median nerve transfers

Neurosurg Focus Volume 42 • March 2017

0–1, respectively. The 2 outcomes associated with nonsurgical management were MRC Grade 4–5 with spontaneous recovery and MRC Grade 0–1 without neurological recovery. Our model grouped all patients with spontaneous recovery to MRC Grades 4–5, a conservative assumption from the cost-effectiveness viewpoint. The corresponding QALYs of each MRC group, obtained from a previous study, were 0.89, 0.82, and 0.81, respectively. Although QOL would be expected to improve between MRC Grades 2 and 3 with the capacity to perform movements against gravity, current literature associates approximately equivalent QALYs to these MRC grades. Our model assumed that equivalent restoration of elbow flexion to a given MRC grade whether by surgical intervention or by spontaneous recovery with nonsurgical management would result in equivalent QALY. Our model also assumed that improving from MRC Grades 0–1 to 4–5 regardless of surgical intervention or spontaneous recovery would result in equivalent likelihood to return to work.

Model Probabilities

Our model assumed that all patients had equivalent deficits in unilateral elbow flexion before making the choice of surgical versus nonsurgical management for their brachial plexus injury. Prior studies that have assessed upper brachial plexus injuries with nonsurgical treatment have demonstrated a 12%–41% chance of recovery of elbow flexion within the first 3 months. If spontaneous neurological recovery was not observed within the first 4.5 months, nonsurgical recovery was modeled to be unlikely over a lifetime. Our model conservatively assumed that even though spontaneous recovery of neurological function did not occur within the first 4.5 months, patients would have a 25% chance to make this degree of recovery in the subsequent 1-year period, a conservative assumption from a cost-effectiveness perspective. According to prior published data on ulnar nerve transfers, the Oberlin nerve transfer demonstrates an approximately 80% success rate, defined as the proportion of patients achieving MRC Grade 4 or higher. In a case series of 6 patients who underwent a double fascicular nerve transfer, the success rate of achieving MRC Grade 4–5 was 100%. Meanwhile, a prospective case series showed that patients who underwent median nerve transfer demonstrated a 73% success rate of achieving MRC Grade 4–5. Given the comparable rates of success between ulnar nerve transfer, median nerve transfer, and combined procedures, our model used the most conservative estimate (73%) of achieving MRC Grade 4–5 after surgical intervention. For the purposes of our model, if good surgical outcome was not obtained, patients had a 90% chance of achieving MRC Grade 2–3. In the remaining 10% of cases, patients did not improve in MRC grade following surgery; these cases were considered surgical failures/poor outcomes.

Rates of surgical complications were derived from a prior study examining complications associated with comparable peripheral nerve surgeries involving the upper extremity. Our model included 2 potential complications of surgery: scar tenderness and wound infection. Our model assumed that these 2 complications were considered independent events. The annual probability of death due to natural causes at any given age was obtained from the US Census Bureau Data (https://www.cdc.gov/nchs/nvss/mortality_methods.htm). All data on the probabilities of transition between functional states and the associated QALYs were collected retrospectively from the literature (Table 1).

Costs

All analyses were performed using a third-party payer’s perspective. Total costs associated with surgery were determined by 2015 Medicare Fee-For-Service payment values (https://www.cms.gov/apps/physician-fee-schedule) using Current Procedural Terminology (CPT) codes with a 2015 conversion factor of $35.80. CPT codes associated with pedicle nerve transfer surgery, facility charges, an-
A. R. Wali et al.

Neurosurg Focus Volume 42 • March 2017

Anesthesia, clinic visit costs, preoperative electromyography (EMG), preoperative cervical spine MRI, and 8 postoperative rehabilitation visits were summed to provide a total cost of $5066.19 with surgical treatment. Components of surgical cost are listed in Table 2.

Brachial plexus injuries and corresponding disabilities contribute substantially to additional costs associated with loss of income and daily living. 11,17 In 2014, Felici et al. demonstrated that patients with brachial plexus injury had a 45% disability rate. After surgery and achieving MRC Grade 4 or 5 elbow flexion, the disability rate decreased to 30%. 12 Using these data, we modeled our probability of return to work at 55% for those with MRC Grade 0–1 and 2–3, and at 70% for patients with MRC Grade 4–5. For those returning to work, we assumed a mean annual income of $48,320 based on the Bureau of Labor Statistics 2015 data (https://www.bls.gov/oes/current/oes_nat.htm).

Analysis

All analyses of the model were performed using TreeAge Pro 2016 (TreeAge Software). Variables were tabulated into our model, and the incremental ICER was assessed. The model discounts utilities 3% annually to adjust for future changes in QOL. 13 The cost-effectiveness of surgical management compared with nonsurgical management was measured with an ICER, which is equivalent to the cost associated with each additional QALY gained. Results were considered cost-effective if the ICER was less than a willingness-to-pay (WTP) cutoff of $50,000/QALY, a convention used in numerous cost-effectiveness studies. 5

Table 1. Parameters used in our cost-effectiveness model

| Parameter | Base-Case Value | SD* | Distribution for Probabilistic Sensitivity Analysis† | Authors & Year |
|-----------|----------------|-----|--------------------------------------------------|----------------|
| Initial age (yrs) | 28 | 5.6 | Binomial | Cho et al., 2014 |
| Probability of good surgical outcome | 0.73 | 0.146 | Beta | Cho et al., 2014 |
| If good outcome not obtained, probability of surgical failure | 0.1 | 0.02 | Beta | Cho et al., 2014; Nath et al., 2006 |
| Probability spontaneous recovery | 0.25 | 0.05 | Beta | Nagano, 1998; Kim et al., 2003 |
| Baseline probability of returning to work with MRC Grade 1–3 | 0.55 | 0.11 | Beta | Felici et al., 2014 |
| Improved probability of returning to work with MRC 4–5 | 0.7 | 0.14 | Beta | Felici et al., 2014 |
| Cost of surgery | $5,066.19 | $1,013.24 | Gamma | Centers for Medicare & Medicaid Services, 2016 (see text) |

| Parameter | Base-Case Value | SD* | Distribution for Probabilistic Sensitivity Analysis† | Authors & Year |
|-----------|----------------|-----|--------------------------------------------------|----------------|
| Mean annual wage | $48,320 | $9,664 | Gamma | Bureau of Labor Statistics, 2015 (see text) |
| Probability of wound infection | 0.09 | 0.018 | Beta | Song et al., 2012 |
| Probability of scar tenderness | 0.09 | 0.018 | Beta | Song et al., 2012 |
| MRC Grade 4–5 QALY | 0.89 | 0.11 | Beta | Ali et al., 2014 |
| MRC Grade 2–3 QALY | 0.82 | 0.11 | Beta | Ali et al., 2014 |
| MRC Grade 0–1 QALY | 0.81 | 0.14 | Beta | Ali et al., 2014 |
| Scar tenderness QALY multiplier | 0.97 | 0.09 | Beta | Song et al., 2012 |
| Wound infection QALY multiplier | 0.92 | 0.03 | Beta | Song et al., 2012 |

* SD derived from literature when applicable; otherwise, 20% of the mean was used to provide SD if the value was not present in the literature.
† Binomial, beta, and gamma distributions refer to probabilistic distributions used in probabilistic sensitivity analysis.

TABLE 2. Components of surgical costs

| Direct Cost Component | Fees* | CPT Code |
|-----------------------|-------|----------|
| Surgery + facility fee | $2,240.89 | 64905 |
| Anesthesia | $670.00 | 01710 |
| New neurosurgery clinic visit | $207.29 | 99205 |
| Pre- & postop surgical visits | $976.32 | 99203 |
| EMG conduction study | $197.62 | 95910 |
| Preop EMG | $92.00 | 95886 |
| Preop cervical spine MRI | $225.57 | 72141 |
| Rehabilitation | $85.57 | 97003 |
| New visit | $370.93 | 97004 |
| Follow-up | $5,066.19 | |

* Fees were derived from the 2015 Medicare Fee-For-Service payment values (https://www.cms.gov/apps/physician-fee-schedule).
tained conservative estimates of the cost-effectiveness and benefits of surgery. Monte Carlo probabilistic sensitivity analysis was conducted with 100,000 iterations.10 Age distributions were modeled as binary distributions. Costs were modeled by gamma distributions to capture a range of costs between zero and infinity. Probabilities and health utilities defined by QOL were modeled after beta distributions between 0 and 1. When possible, standard deviations associated with given values were obtained from the literature. When standard deviations were not available, a 20% standard deviation was assigned to the mean. Given the high variance associated with QALYs and MRC grade, Monte Carlo probabilistic sensitivity analysis was performed with and without taking into account the differences due to variance among MRC grades.

Results

Base Case Analysis

Our model demonstrated that surgical intervention is strongly effective, yielding 21.23 QALYs in the surgical group compared with 20.44 QALYs with nonsurgical management. Our cost-effectiveness analysis showed that surgical management was cost-effective with an ICER of $6453.41/QALY when not including potential income recovered through returning to work with MRC Grade 4–5 elbow function. When considering potential lifetime income gained with improved elbow function at MRC Grade 4–5 elbow function, surgical management was cost-effective with an ICER of −$96,755.42. This negative ICER indicates that, despite costs associated with surgery, the potential income recovered through returning to work may result in monetary gain.

One-Way Sensitivity Analysis

Cost-effectiveness was most sensitive to changes in cost of surgery, probability of good surgical outcome, and probability of spontaneous recovery. Changes in cost of surgery from $5000.00 to $50,000 yielded ICERs ranging from $6369.10 to $63,690.98/QALY. Regardless of the potential income earned over lifetime due to a successful functional outcome, ulnar and median nerve transfer demonstrated cost-effectiveness up to a threshold cost of $39,252.03. Changes in probability of good surgical outcome (MRC Grade 4–5) from 50% to 100% yielded ICERs between $4008.00 to $13,437.40/QALY gained, demonstrating cost-effectiveness irrespective of the income gained through returning to work at a willingness to pay of $50,000/QALY gained. Chances of spontaneous recovery in the nonsurgical group in the year following the initial 4.5 months of injury without spontaneous recovery were modeled between 0% and 60%, resulting in ICERs that ranged from $4026.68 to $41,295.72, again demonstrating cost-effectiveness (Table 3).

Two-Way Sensitivity Analysis

Two-way sensitivity analysis (Fig. 3) illustrated the most cost-effective strategy, with surgical costs ranging from $5066.19 to $50,000 and probability of good surgical outcome ranging from 50% to 100%. For the surgical treatment to be the more cost-effective strategy at the WTP cutoff, the cost of surgery must not exceed $18,851.08 where success of achieving MRC Grade 4–5 is 50%. Moreover, surgical intervention can remain cost-effective for up to $50,000 when surgical success rate is 85% or greater. When accounting for possible income gained with improved elbow function, nerve transfer surgery was found to be cost saving, yielding an ICER within a WTP cost ranging from $5066.19 to $50,000. Even our most conservative parameters in which probability of surgical success was 50% and cost of surgery was $50,000 yielded an ICER of $18,828.06/QALY, demonstrating cost-effectiveness.

Probabilistic Sensitivity Analysis

Monte Carlo probabilistic sensitivity analysis of 100,000 iterations, with surgical success and spontaneous recovery probabilities, QALYs, potential income lost due to disability, and cost of surgery modeled as distributions to account for variations, showed that surgical intervention is more cost-effective than nonsurgical management in 76% of cases at the WTP cutoff (Fig. 4).

| Parameter | Value Used for Sensitivity Analysis | ICER ($/QALY gained), Disregarding Income Loss w/ Disability |
|-----------|------------------------------------|-------------------------------------------------------------|
| Cost of surgery* | $5,000.00† | $6,369.10 |
| | $16,250.00 | $20,699.57 |
| | $27,500.00 | $35,030.04 |
| | $38,750.00 | $49,360.51 |
| | $50,000.00 | $63,690.98 |
| Probability of good surgical outcome | 50% | $13,437.40 |
| | 60% | $9,137.80 |
| | 70%‡ | $6,922.72 |
| | 80%§ | $5,572.02 |
| | 90%¶ | $4,662.34 |
| | 100%** | $4,008.00 |
| Probability of spontaneous recovery after 4.5 mos w/o neurological improvement | 0% | $4,026.68 |
| | 10% | $4,739.59 |
| | 20% | $5,759.24 |
| | 30% | $7,337.86 |
| | 40% | $10,108.68 |
| | 50% | $16,241.62 |
| | 60% | $41,295.72 |

* Nerve transfer surgery remained cost-effective across the ranges of surgical cost (threshold of cost-effectiveness: $39,252.03), probability of good surgical outcome, and probability of spontaneous recovery.
† The approximate cost of a nerve transfer procedure in this study was $5,066.19.
‡ Cho et al., 2010: approximate success rate of median nerve transfer (73%) based on retrospective data.
§ Mackinnon et al., 2005: approximate success rate of Oberlin procedure based on meta-analysis.
¶ Nath et al., 2006: approximate success rate of median nerve transfer.
** Mackinnon et al., 2005: approximate success rate of double fascicular transfer based on a meta-analysis.
Discussion

Quantification of outcomes is a cornerstone of evidence-based medicine. Surgical interventions are increasingly scrutinized, and outcome measurements are constantly being refined. The ultimate outcome of interest for patients is QOL, and, in our progressively cost-conscious health care system/society, it is imperative to identify treatments that are cost-effective in improving QOL.

In previously published studies, median nerve transfer, ulnar nerve transfer, and a combination of ulnar and median nerve transfer in patients with upper brachial plexus injury have been demonstrated to be effective surgical strategies for restoring elbow flexion.\textsuperscript{16,19} We present the first study, to our knowledge, to assess the cost-effectiveness of the procedures. Despite the small chance of spontaneous recovery in upper brachial plexus injuries after 4.5 months of injury,\textsuperscript{19} our model demonstrated that surgical intervention is highly cost-effective compared with conservative management for improving the QALYs for patients with upper brachial plexus injury while also increasing the likelihood that a patient may return to work and earn income over lifetime. Both the increase in income and the improvements in QALY across a lifetime through surgical intervention made nerve transfer surgery cost-effective at a WTP of less than $50,000/QALY even at the most conservative estimates of a 50% chance of surgical success and $50,000 cost of surgery.

Our study demonstrated a negative ICER (~$96,755.42/QALY) when modeling the income lost due to elbow flexion disability and the increased probability of a patient returning to work after a good surgical outcome. This highlights that the magnitude of potential income gained through improving elbow function exceeds the costs of nerve transfer surgery. Importantly, the result of this study demonstrates the cost-effectiveness of the Oberlin nerve transfer and comparable procedures utilizing the median nerve, ulnar nerve, or a combination of both.\textsuperscript{5,16,19}

There are several limitations to our model. This model is based on assumptions and values obtained from prior studies, many of which are retrospective single-center studies that have not been externally validated in prospective, randomized trial settings. The costs of surgery used in this study were derived from Medicare values and may not capture costs across different health care settings. Probability of success may vary from surgeon to surgeon and certain facilities may not offer nerve transfer surgery. Our model does not incorporate additional costs associated with surgical complications, other types of surgical complications, or other ancillary surgical costs including cost of pain medications and antibiotics. However, the range of surgical costs in our 1-way and 2-way sensitivity analyses accounted for additional costs that were not included and demonstrated that surgical intervention is cost-effective up to $18,851.08 at a good surgical outcome rate of only 50% and cost-effective up to $50,000 for surgical costs with a good surgical outcome rate of 85%. When considering the potential income recovered through returning to work, surgical intervention was cost-effective across the entire range of surgical cost from $5066.19 to $50,000 and the entire range of probability of good outcome from 50% to 100%.

Our model does not take into account possible neurological injury as a complication associated with surgery. Oberlin in 1996 reported postoperative weakness after nerve transfer surgery, but the weakness was not permanent.\textsuperscript{23} Moreover, the decrease in QALY associated with functional loss due to fascicular injury of the median or ulnar nerve is not yet established within the literature, limiting our cost-effectiveness model from analyzing surgical complications that may decrease function. Another limitation was the large variance in QALYs at a given MRC grade,\textsuperscript{2} which could suggest potential scenarios in which patients with MRC Grade 4–5 functionality have a lower QALY than patients with an MRC Grade 0–1. Large variance in QALYs across MRC grades highlights the importance and need for more preference-based QOL research to lay the foundation of more precise research in medical decision-making. Despite this large variance, surgical intervention remained the more cost-effective choice in 76% of iterations through Monte Carlo probabilistic simulation, highlighting the utility of nerve transfer surgery over conservative management alone. Future studies are needed to identify and validate precise QALY values associated with different MRC grades of elbow flexion function.

Despite these limitations, this study provides an important perspective for the role of the median nerve transfer, ulnar nerve transfer, or a combination of both for upper
brachial plexus injury. In the absence of spontaneous neurological recovery within 4.5 months of the initial nerve injury, these surgical procedures are cost-effective compared with nonsurgical management to restore elbow flexion after upper brachial plexus injury. These findings should be considered when recommending potential surgical candidates to receive nerve transfer surgery.

Conclusions

Upper brachial plexus injury can result in loss of elbow flexion, leading to disability and reductions in QOL. Our study demonstrates that Oberlin nerve transfer and similar procedures are highly cost-effective strategies for restoring elbow flexion function and improving QOL for patients with upper brachial plexus injury.

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**Disclosures**
The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

**Author Contributions**
Conception and design: all authors. Acquisition of data: Mandeville, Wali, Park. Analysis and interpretation of data: Mandeville, Wali, Park. Drafting the article: Mandeville, Wali, Park. Critically revising the article: all authors. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript: all authors. Administrative/technical/material support: Mandeville.

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