Using Decision Analysis to Understand the Indications for Unilateral Hand Transplantation

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Abstract

Background: Upper extremity transplantation has been performed to improve quality of life, the benefit which must be traded off for the risk created by life-long immunosuppression. We believe the process of decision analysis is well suited to improve our understanding of these trade-offs. **Method:** We created a decision tree to include a branch point to illustrate the expected recovery of useful function in the transplant, using the best estimates for utility and probability that exist. **Results:** Our model revealed that when the probability of achieving a good result, graded as Chen level one or two is greater than 73%, transplantation is preferred over no transplantation. The decision is sensitive to the probability of major complications and the utility of a transplanted limb with minimal function. **Conclusions:** The results of this analysis show that under some circumstances given a high probability of satisfactory functional recovery, unilateral hand transplantation can be justified.

Keywords: hand transplantation, decision analysis, unilateral, utility, quality of life

Introduction

Vascularized composite allograft (VCA) is used to improve quality of life through improved function and reduction of suffering. Although this holds promise for many patients, the indications for upper extremity transplantation have not been clearly elucidated. In addition to the limited worldwide experience, we think this is likely due to the complexity of the patient population and the difficulty in measuring outcomes. The population presenting with the potential need for upper extremity transplantation is heterogeneous including patients with unilateral or bilateral injuries, varying levels of amputation, varying mechanisms of amputation, and a plethora of other demographic and co-morbid variations. Measuring the outcome of VCA is challenging because no outcome instrument or single or group of physical measures can capture the multiple domains involved.⁵ We have been interested in using decision analysis to evaluate the merits of upper extremity transplantation, seeing it as a way to weigh the multiple risks and benefits of the procedure, the expected outcome, and the risks of immunosuppression.

In 1998, a decision analysis comparing transplantation with no transplantation was published before hand transplantation was a clinical reality.⁶ This simple decision tree model clarified the preeminent importance of reducing the probability and severity of complications of immunosuppression rather than survival of the transplanted hand. This decision model also found that in the base case, using the assumptions

made, transplantation of a hand in a patient with a unilateral amputation was not recommended (Figure 1).

A second decision analysis was later published in 2010 evaluating cost and expected value in unilateral and bilateral hand transplantation (Figure 2).³

This analysis revealed that bilateral transplantation had a higher expected value than no transplantation and supported the earlier study showing in the base case that unilateral transplantation was not recommended. Both of these models considered the possibility of survival or failure of the transplant and the potential for immunosuppression-induced morbidity. Neither model however included a modification of the expected value based on the functional recovery of the transplanted extremity. Now that experience has been gained in upper extremity transplantation, and a high rate of survival is anticipated, close attention can be turned to the quality of functional recovery. As functional recovery is purported as the purpose of upper extremity transplantation and has been highly variable in upper extremity transplants and replants, the inclusion of this into a decision model seems critical. Furthermore, the probability of events can be refined based on experience. If good functional

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Figure 1. Early decision tree for unilateral hand transplantation, as per McCabe et al (1998).

Figure 2. First-generation decision tree for unilateral hand transplantation, as per Chung et al (2010).

recovery can be anticipated, the indications for transplant will be enhanced; however, if poor functional recovery is anticipated, the indications for transplant will be limited.

There is no standard method to evaluate structure in decision models. It is important that decision models capture the critical elements of patient management so that clinicians will recognize and believe in the results. If the models are too complex, however, they may be difficult to understand and not be widely accepted. One method to evaluate model structure is to vary the structure of the model, perform the analyses, and then compare the results for differences. We follow this logic to modify the decision models in the literature to include the quality of functional recovery and compare the results with those published models.

In replantation surgery, the probability of good functional recovery has been linked to patient and injury factors such as the level of amputation,² age, and mechanism of injury.⁸ Extrapolating to transplantation, it is possible that consideration of the anatomic level of amputation and possibly other prognostic factors in the decision model can be used to refine the analysis to reflect the current state of knowledge. It is our belief that with good quality models, the use of decision modeling in upper extremity transplantation may be the best method to further develop the indications for the procedure.

The purpose of this study was to extend previously published decision models, adding a modification to include the concept of functional recovery. If relevant, our secondary

Figure 3. Second-generation decision tree for unilateral hand transplantation.

purpose is to study this expanded model to further understand and make recommendations regarding the indications for upper extremity transplantation.

Method

We started with the 2 published models for upper extremity transplantation (Figures 1 and 2), modifying these models to include a branching point for the quality of the functional result (Figure 3). For the initial exploration of this comparison between the published models and our new model, we dichotomized functional result into satisfactory and unsatisfactory. To do this, we used the scale proposed by Chen to quantify the quality of the result following limb replantation (Table 1).² For the purposes of our decision model, we rated a Chen score of 1 or 2 as satisfactory and a Chen score of 3 or 4 as unsatisfactory. We made assumptions about the probability of achieving a satisfactory result for transplantation by using the probabilities of achieving a Chen level 1 or 2 with replantation at various levels as published by Chen. We focus this report on the decision for unilateral transplantation.

Following creation of the revised model structure, we used utility and probability values from the literature when

Table 1. Chen's Score for Functional Recovery After Replantation.

Chen's score	Functionality
1	Able to resume original work Range of Motion exceeds 60% of normal Complete or nearly complete recovery of sensation Muscle power of grades 4 and 5
2	Able to resume some suitable work Range of Motion exceeds 40% of normal Nearly complete recovery of sensation Muscle power of grades 3 and 4
3	Able to carry on normal life Range of Motion exceeds 30% of normal Partial recovery of sensation Muscle power of grade 3
4	Almost no function of survived limb

possible. To test the robustness of the models, we performed multiple sensitivity analyses.

Using the results of our models and the previous publications, we created a rank order list of indications for upper

Table 2. Base Case Utilities.

Scenario	Utility ^a
Unilateral hand amputation	
No hand transplant	
Prosthesis	0.75
Hand transplant	
Well with functionally successful result	0.80
Well without functionally successful result	0.76
Ill with functionally successful result	0.61
Ill without functionally successful result	0.57
Graft failure	0.73

^aA rating of 1.0 indicates perfect health.

extremity transplantation. To do this, we followed the structure put forward by the American Heart Association Council on Cardiovascular Disease in the Young and the Councils on Clinical Cardiology, Cardiovascular Nursing, and Cardiovascular Surgery and Anesthesia.¹

Results

Tree Structure

On close inspection, it is noted the structures of the two published decision models for upper extremity transplantation were fundamentally the same. Both models have a decision node for “transplantation” and “no transplantation.” In Chung’s model, the “no transplantation” node includes prosthetic wear. We omitted the branch for death in Chung’s model. “Ill health” and “well” in the original decision model can be construed as the same as “major” and “minor” complications in Chung’s model. We will call this model structure the “first generation” decision model. We created an expansion of this model adding a branching point for the functional quality of the outcome (Figure 3) dichotomizing the result into functionally successful, Chen 1 or 2, and not functionally successful, Chen 3 or 4. Decision models will typically have a branch point for efficacy and one for complications. We call this the “second generation” decision model for upper extremity transplantation. We used the table from Chen’s reference to estimate the probability of achieving these results at various anatomic levels. For example, for transplantation at the wrist, we assumed the probability of achieving a Chen 1 or 2 functional outcome would be 80%. At the level above the elbow, we assumed the probability of Chen 1 or 2 would be 50%. For the utilities of good or poor results, we used the published numbers from Chung’s model for the base case.

To distribute the utility for a good and poor functional result, we made the following assumptions. For a patient with mild morbidity from immunosuppression and a good functional result, we increased the value of the published utility, and for mild morbidity from immunosuppression with poor

functional result, we decreased the utility by a similar amount. We made a similar assumption for the utilities when there were major problems with immunosuppression (Table 2). We assumed the probability of loss of the transplant is 5%, and for the base case scenario, we assumed the probability of having major morbidity from immunosuppression would be 20%. These probabilities are slightly different from those published by Chung, and although they are not precisely defined, we believe they reflect the probabilities in the literature.^{3,7}

Analysis

The model is analyzed by a simple process called “folding back.” To calculate the expected value of our decision model alternatives, we multiply the utility of a final state of health by the conditional probability of achieving that state being achieved, yielding the probability weighted utility, also called the expected value of that state of health. The expected values of alternatives emanating from each node are added yielding the expected value of that node. This is repeated from right to left in a process called folding back. This folding back will reveal the preferred decision choice as the one with the highest expected value.

Following the base case analysis, the various utility and probability values were changed through a reasonable range of possibilities and the analysis repeated. This sensitivity analysis can illustrate the robustness of the result of the analysis, can point to the need for more precision in measurement, and can provide information for further inference. For example, changing the probability of achieving a good functional result from 50% to 80% can represent the decision for performing a transplant above the elbow versus the wrist level.

Base Case Analysis

Using our second-generation model of unilateral transplant and a 50% probability of achieving a satisfactory functional result, the result of the base case analysis suggested that no transplant was the preferred alternative. When the probability of achieving a good functional result (Chen 1 or 2) was increased to 80%, transplantation became the preferred option. Using the sensitivity analysis, we determined the threshold for this probability of achieving a satisfactory result was 73%. In other words, using the assumptions we have made, if the probability of achieving a Chen level 1 or 2 level of function after a unilateral transplant is greater than 73%, our model shows this is the preferred option to no transplant. For those unilateral situations when there is a low probability of achieving a good functional result, this model suggests that transplant is not preferred. Given this threshold for the transplant decision, the surgeon can evaluate the anatomy of the injury and determine to the best degree possible how likely the patient will achieve good function. Clearly the level of amputation is one important factor that must be considered.

The probability of major “complications” was set at 20% for the base case. When this was changed to 10%, the expected value for transplant in the unilateral situation increased with the model showing a preference for unilateral transplant with a threshold of 58%.

This result is sensitive to the utility of the transplanted limb when it has minimal function, a quantity that is not clearly defined in the literature. If we make the assumption that a patient has a strong preference for the presence of a transplanted limb, even with poor function, our result could be interpreted as being too conservative. If, however, the preference for the transplant outcome depends on a reasonable functional recovery, a position most surgeons would advocate for, we believe our decision model results are accurate and applicable.

Discussion

In our second-generation model, we have been able to show that unilateral transplantation can be preferred to no transplantation under some circumstances. Our model shows that the probability of achieving a good functional result has an important role to play in unilateral transplantation decisions. If the probability of achieving a good functional result, one that we have defined as a Chen level 1 or 2, is estimated at greater than 73%, then unilateral transplantation of the upper extremity could be the preferred option. Using the assumptions we have made, we now believe that situations when a good functional result can be anticipated, such as unilateral amputation at the level of the wrist, are valid indications for unilateral transplantation. When the probability of a good functional result drops, the decision for transplantation in the unilateral case is not supported by this model. For our base case analysis, we used a probability of survival of the transplanted hand of 95%.⁷ When the probability of major complications was changed from 20% to 10%, the expected value for transplant in the unilateral situation increased with the model showing a preference for unilateral transplant with a threshold of 58%. As experience is gained, the probability of major complications will be known with greater precision.

One critical piece of information that is not currently available is the utility or strength of preference a patient will place on a living transplanted arm with little to no function. As surgeons, we believe this state of health would not compensate for the risk of immunosuppression. The differing perspectives of surgeons and patients regarding hand transplantation have been extensively discussed.⁴ Another important factor not considered in these models is the potential for removal of the transplant after 2 to 3 years if functional recovery is not satisfactory for the patient or if the burden of immunosuppression is too high. This “trial of transplant” concept suggests that our model may be too conservative and has the potential to increase the indications for the procedure. Measurement of the morbidity of a failed attempt at transplant compared with

the regret of not attempting the procedure would seem to be a fruitful area for comparison.

Indications for upper extremity transplantation are ill defined. Because of the small number of cases performed and the difficulty in evaluation of the outcome, it will take a long time for experience to guide us. Decision analysis is a method designed to help make the best decision in the face of uncertainty. When combined with utility, a measure of the patients’ preference for a state of health, decision analysis seems well suited to assist in our understanding of the indications for upper extremity transplantation.

Given our current understanding of the potential functional recovery after upper extremity transplantation and the uncertainty surrounding the patients’ preference for some of the important states of health, we searched for a method to describe the indications for upper extremity transplantation. We wanted to reflect current knowledge, incorporate the results of our analysis, but allow for uncertainty where it existed. In the literature review, we found “A Scientific Statement From the American Heart Association Council on Cardiovascular Disease in the Young; the Councils on Clinical Cardiology, Cardiovascular Nursing, and Cardiovascular Surgery and Anesthesia” detailing the “Indications for Heart Transplantation in Pediatric Heart Disease.” The structure of this statement detailing the indications for heart transplant seemed to be well suited to upper extremity transplantation and was adopted. This rank order serves as a framework for evaluation and discussion, and we anticipate it will be modified with ongoing experience. The statement lists a rank order of indications based on evidence and expert opinion:

Class I: Conditions for which there is evidence and/or general agreement that heart transplantation is useful and effective.

Class II: Conditions for which there is conflicting evidence or a divergence of opinion about the usefulness/efficacy of heart transplantation.

Class IIA: Weight of evidence/opinion is in favor of usefulness/efficacy.

Class IIB: Usefulness/efficacy is less well established by evidence/opinion.

Class III: Conditions for which there is evidence and/or general agreement that heart transplantation is not useful.

This structure creates a template for discussion and research and can be modified as experience and research progresses. It appealed to us for several reasons:

1. It is already in the literature and deals with another complex transplantation so we did not have to start from scratch.
2. It is complex enough to deal with the multiple clinical scenarios that are presenting themselves for consideration for upper extremity transplant.

3. It reflects current knowledge in a way that can be modified as the discipline advances.
4. It is flexible enough to allow for differing opinions when the evidence is not strong.

We applied these “classes” of indications to upper extremity transplant as follows.

Class I

Bilateral amputation at wrist or distal forearm
 Bilateral amputation with 1 limb at wrist or distal forearm level
 Unilateral amputation at wrist or distal forearm level with severe functional limitations of the opposite hand

Class IIA

Unilateral amputation with privileged immunologic situation
 Bilateral amputation at level with good potential for functional recovery
 Amputation of upper and lower extremities (upper limb transplant only)

Class IIB

Unilateral amputation at wrist or distal forearm level in well-informed, highly motivated individual
 Unilateral amputation with favorable situation for potential good recovery in well-informed, highly motivated individual

Class III

Unilateral upper arm amputation
 Amputation with little potential for functional recovery based on the mechanism of injury, level, other patient factors
 High risk of severe morbidity from immunosuppression

We believe this framework creates a structure for discussion and further research and anticipate it will be modified as further experience is gained.

The limitations of this study are predominantly related to the uncertainty surrounding our decision analysis. This can be broken into 3 components. A tree model has limitations when trying to simulate the states of health involved. For example, the tree model does not easily allow for transitions between these multiple states. More complex microsimulations can be used to overcome this problem.

The probability estimates are based on limited samples and will be refined through experience. Utility is a method to measure the preference for specific health states. This

measurement originates in health economics and is not widely used in the hand literature. The use of utility to measure the states of health in upper extremity transplantation is limited, and surgeons may lack confidence in its use.

Ethical Approval

This study was approved by our institutional review board.

Statement of Human and Animal Rights

This article does not contain any studies with human or animal subjects.

Statement of Informed Consent

This article does not contain any studies with human or animal subjects.

Declaration of Conflicting Interests

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