Targeted Muscle Reinnervation Does Not Increase the Risk of Postsurgical Complication or Overall Cost

Sorka T. Deeyor, BS*
Haroon M. Kisana, MS*
Clayton H. Hui, BSE*
Chad Stecher, PhD†
Joshua W. Hustedt, MD, MHS*

Background: Targeted muscle reinnervation (TMR) has shown promise in reducing postsurgical limb pain in amputees. However, there has been little evidence on the increased risk of complications and cost as compared with traditional amputations. This study was designed to assess the rate of complications and healthcare costs between those treated with TMR and traditional amputations.

Methods: Patients undergoing amputation were selected from the PearlDiver Mariner dataset and categorized into one of two treatment groups depending on the use of TMR versus traditional amputation. Rates of postsurgical complications and overall healthcare costs were compared between the two groups, while controlling for differences in patient demographics and comorbidities.

Results: One hundred sixteen TMR procedures and 76,412 traditional amputations were included in the study. The rate of complications did not differ between groups, with a complication rate of 77% in the TMR and 87% in the traditional amputation groups. Overall healthcare costs also did not differ 1 year after surgery, with an average cost of $32,632 in the TMR group and $36,219 in the traditional amputation group.

Conclusions: Amputees experience high rates of postsurgical complications, morbidity, and mortality. However, there is no increased risk of complications or cost with the use of TMR. TMR has the potential benefits of reducing overall postsurgical pain and reestablishing activities of daily living. Although TMR is more expensive up front, it may reduce the overall healthcare costs by reducing the need for subsequent care. Further work is needed in large, randomized trials to examine these findings. (Plast Reconstr Surg Glob Open 2022;10:e4488; doi: 10.1097/GOX.0000000000004488; Published online 24 August 2022.)

INTRODUCTION

Targeted muscle reinnervation (TMR) has shown significant promise in reducing neumora and phantom limb pain in amputees. This promise of reduced pain has significant implications for the nearly 200,000 new amputation cases that occur in the United States each year. Amputee patients face a long, hard recovery, with nearly 75% reporting neumora pain and 85% reporting phantom limb pain after surgery. For many patients, an amputation is the beginning of the end of life, as chronic pain sets in, and the patient no longer ambulates; 5-year mortality for amputees in the United States is around 75%.

So, it is exciting that many TMR papers have been arriving with data to address this monumental surgical and societal challenge. Yet, despite the promise of early studies, questions remain. The original reports of TMR were done primarily in young, healthy, traumatic amputation patients. These studies showed large reductions in neumora and phantom limb pain, with rates of limb pain falling from 75% to 0% and phantom limb pain reducing from 85% to 7%. Over time, TMR indications were expanded to oncological, vascular, and diabetic patients. Most recently, TMR has been shown to be successful in highly comorbid patients, who, despite high comorbidity burden, have experienced large reductions in limb pain.

Yet despite mounting evidence, there have been no large, randomized trials in TMR, and there has been no discussion on the overall costs of the procedure and its associated health policy implications. Proponents of TMR point to its massive reduction in residual limb pain and its associated reduction in patient mortality rates. But

Disclosure: The authors have no financial interest to declare in relation to the content of this article.
opponents argue that there is no randomized data to support its use; that the procedure increases operative time and, therefore, complications; and that the increased costs of the procedure do not yield long-term societal and patient benefits. We designed a study to compare the long-term complication profiles and overall costs of TMR versus traditional amputation in a national dataset to explore the potential benefits and downsides of TMR. These data may help guide future studies of widespread use of TMR in the general population.

MATERIALS AND METHODS

The PearlDiver Mariner dataset was used for this study. The Mariner dataset is a large, national dataset of health insurance claims in the United States. The Mariner dataset contains the health claims data of more than 90 million patients and is one of the largest, publicly available datasets in the United States. We selected all patients who underwent an upper or lower extremity amputation between 2015 and 2020 and categorized them into TMR versus traditional amputation based on common procedural coding for amputations with or without nerve transfers (see appendix for full list of common procedural coding [CPT] codes in the study). To be included in the study, all patients had to be active for 1 year postoperatively in the dataset (1-year “follow-up”).

The primary outcome of interest was the presence of any postsurgical complication. PearlDiver has a preset complication profile coding system that identifies International Classification of Diseases (ICD)-10 codes associated with common postsurgical complications. We searched for complications, including acute kidney injury, infection, cardiac arrest, deep venous thrombosis, wound dehiscence, hematoma, nerve injury, pneumonia, pulmonary embolism, need for blood transfusion, and urinary tract infection. This methodology has been previously used for PearlDiver health claims studies. Patients were categorized as having or not having complications based on having one or more of the individual complications.

Our secondary outcome of interest was overall costs of care. PearlDiver is unique in that it provides outcomes for patients’ overall care as reported through the insurer. These insurance-based data ensure that the costs reported are actual costs and not charges, as reported in other health claims datasets. This distinction provides accurate, market-driven cost data. We analyzed the overall healthcare costs of amputees, who were treated with TMR and traditional amputations 1 year after surgery.

Demographic data were also included for each patient. Age, gender, and Charlson comorbidity index (CCI) were collected for each patient. CCI was chosen as a marker of the overall health of each patient to control for patient variability in health in multivariate analyses.

Statistical analyses were conducted in R. First, patient demographics were compared between the TMR and traditional amputation groups using the t-tests and chi-squared tests. Second, individual and overall complications were compared between groups with chi-square analysis. Third, 1-year mean hospital costs were compared between groups with t-tests. Multivariate regression analysis was then conducted with controls for age, gender, and CCI to isolate the independent factor of TMR on outcomes and cost. A multivariate logistic regression was used to compare the presence or absence of postsurgical complications between groups. The multivariate model provided the odds of sustaining a postoperative complication based on a TMR versus traditional amputation surgical choice. A linear regression model was used to compare the overall healthcare cost at 1 year between TMR and traditional amputation. The study was provided exemption status from institutional review board approval due to the use of deidentified, publicly available data. There was no external source of funding for the study.

RESULTS

A total of 76,528 patients were found to have undergone amputation in the Mariner dataset. One hundred sixteen patients had a TMR procedure, and 76,412 had a traditional amputation. Upper extremity amputees were more likely to receive a TMR procedure, with 29% of TMR cases being performed in the upper extremity (34 of 116 cases), as compared with only 1.7% (1311 of 76,412) of traditional amputations being upper extremity cases ($P < 0.001$; Table 1). TMR patients were also younger (49 versus 65 years; $P < 0.001$), healthier (CCI, 4.03 versus 5.52; $P < 0.001$), and more commonly women (43.1% versus 35.7%; $P < 0.001$; Table 2).

There was no statistically significant difference in overall complication rates between the two groups. Complication rates were high in both groups with 77% in the TMR group and 87% in the traditional amputation group ($P = 0.04$). After controlling for gender, age, and CCI in a multivariate logistic model, the risk of experiencing a postoperative complication during a TMR procedure was not significantly different from a traditional amputation (OR, 0.74; $P = 0.198$; Table 3).

Overall costs for TMR and traditional amputations did not differ at 1 year ($32,632 versus $36,219; Table 4). The difference in cost between the two procedures was not found to be significantly predicted by choice of TMR, after controlling for age, gender, and CCI ($P = 0.719$; Table 5).

Takeaways

**Question:** What is the effect of targeted muscle reinnervation (TMR) on complications and cost following an amputation?

**Findings:** TMR does not increase the risk of complications or increase overall healthcare costs as compared with traditional amputations.

**Meaning:** TMR may yield long-term cost savings by reducing narcotic use and enhancing patients’ return to function without increased rate of complications as compared with traditional amputations.
DISCUSSION

This study found no difference in complication rates or overall costs between patients treated with TMR or traditional amputation. In the dataset, patients treated with TMR experienced complications 77% of the time as compared with 87% of the time in traditional amputation. In addition, the overall average costs of care at 1 year were similar between the two groups.

The findings of this study show that the majority of complications and costs are likely arising from the initial need for the amputation procedure and not from an additional nerve transfer procedure at the time of the reconstruction. This finding is important as the addition of nerve transfer procedures, such as TMR, has been shown to significantly reduce the overall risks for postoperative neuroma formation and phantom limb pain. Two major critiques of the widespread adoption of TMR for amputation have been the thought that increased operative time from the nerve transfer could potentially increase risks of complication and would also increase the overall costs of care. This study suggests that this may not be the case in the overall population.

The interpretation of large datasets has certain limitations that are important to discuss. We chose to design this study to examine the outcomes of patients undergoing TMR versus traditional amputation. Determining the operative procedural difference between these groups in a large healthcare dataset is relatively simple and reproducible, because it utilizes common procedural coding terminology (CPT 64905 suggests nerve transfer was conducted in addition to amputation). Use of CPT codes to determine groups has been shown to be reliable in insurance claims datasets. However, determining the reason for the amputation (ie, vascular compromise, trauma, or diabetes) is less reliable, as it relies on the use of ICD-10 coding. Accurate CPT coding is required for the operative surgeon to be paid for the procedure, but accurate ICD-10 coding is not. This is a limitation of any large insurance claims data. In exchange for this limitation, the dataset provides strength with numbers and accurate overall healthcare costs.

Given these limitations, we elected to utilize multivariate regression models as our primary outcome measure. These models allowed us to isolate the effect of a TMR procedure and to compare it independently to a traditional amputation. We found that patients undergoing TMR tended to be younger (49 versus 63 years; \( P < 0.001 \)) and healthier (CCI, 4.03 versus 5.52; \( P < 0.001 \)). To control for this, we chose to utilize the Charleston comorbidity index, a standardized approach to overall health in large claims data, and utilized a multivariate regression approach. The multivariate regression provided independent data on the effect of TMR as compared with traditional amputation. We believe that this statistical approach is a better approach than utilizing ICD-10 coding, as ICD-10 coding has been shown to be inaccurate in large claims data.

We found that complications are common in amputees, but that they did not differ with the addition of a TMR procedure in comparison to a traditional amputation. 77% of TMR patients and 87% of traditional amputation patients experienced at least one postsurgical complication. After controlling for age, gender, and comorbidity, the odds of sustaining a complication were not statistically significant between the groups. Our results are similar to those from Chang et al7 in which they found similar rates of wound complications between TMR and traditional groups, even among highly comorbid patients. However, these results also examine the overall health outcomes beyond wound complications, suggesting TMR does not increase the general overall health risk to patients undergoing the procedure.

Table 3. Results of Logistic Regression Model Examining the Risk of Sustaining Any Postoperative Complication

| Variable | Odds Ratio | Std Error | \( P \) |
|----------|------------|-----------|-------|
| TMR procedure | 0.74 | 2.54 e – 01 | 0.198 |
| Age | 1.01 | 7.91 e – 04 | <0.001 |
| Gender (male) | 0.7 | 2.41 e – 02 | <0.001 |
| CCI | 1.32 | 4.44 e – 03 | <0.001 |

Table 4. One Year Healthcare Costs between Those Treated with TMR and Traditional Amputation

| Group | Mean | Median | Standard Deviation |
|-------|------|--------|-------------------|
| TMR | $32,652.20 | $18,954.90 | $36,063.09 |
| Traditional amputation | $36,219.39 | $12,052.00 | $119,947.90 |

Table 5. Results of Linear Regression Model Examining Overall Healthcare Costs at One Year

| Variable | Coefficient | Standard Error | \( P \) |
|----------|-------------|---------------|-------|
| Age | –3.55 e – 05 | 1.07 e – 05 | <0.001 |
| Gender | 2.97 e – 04 | 2.85 e – 04 | 0.295 |
| CCI | 2.25 e – 04 | 3.72 e – 05 | <0.001 |
| TMR | 1.25 e – 03 | 3.49 e – 03 | 0.719 |
Interestingly, we found no difference in overall healthcare costs between groups at 1 year. The average healthcare cost for a patient in the TMR group was $32,632 versus $36,219 in traditional amputation, and the distribution of costs was also very similar. The presence of a TMR procedure did not significantly increase the cost of healthcare even after controlling for age, gender, and CCI. We feel this is an extremely important finding. A TMR procedure includes multiple nerve transfers, which increases the immediate costs of care. However, the overall 1-year cost did not differ. This suggests that the initial investment of a TMR procedure may yield long-term cost savings by reducing the use of narcotic medication, increasing the likelihood of ambulation, reducing the presence of chronic pain, and more successfully returning a patient back to their activities of daily living. This return to function may significantly reduce the overall morbidity, mortality, and cost of care following amputation.

TMR certainly has a growing body of literature to support its use, and our results suggest that it is associated with a similar complication and cost profile. There is significant upside for patients’ long-term function, and TMR offers many benefits and promise. Yet is TMR ready for widespread use? Unfortunately, to date, there has been only one small, randomized trial that ended recruitment early.9 The small numbers in the study are likely due to TMR being restricted to young, healthy, traumatic amputation patients. We believe that in order for TMR to be considered for widespread use, we need to conduct simple, large, randomized trials in highly comorbid patients. If we do so, and the results hold, TMR may offer significant benefits for most patients following amputation.

As the popularity of TMR increases, the need for coordination of care will increase. At many institutions, the surgeons trained in TMR techniques are plastic, orthopedic, or neurosurgeons, while many amputations are performed by vascular or general surgeons. The coordination of these teams will be crucial in identifying and providing TMR. In addition, many amputations are performed in a community setting where a peripheral nerve expert may not be present, and a patient would need to be transferred to undergo the procedure. Future studies may need to examine the practicality of coordinating TMR care and examine the financial implications of doing so in comparison to the clinical outcomes.

Overall, our findings suggest that TMR has a similar complication and cost profile. If the current results with TMR hold in larger, randomized trials, TMR may be a significant path forward for the 200,000 patients undergoing amputations in the US each year. The prospect of addressing the large percentages of postsurgical pain and high mortality rate is certainly appealing, and it appears that the upfront costs of TMR may yield reduced healthcare spending in the long run by reducing postsurgical need for additional care. Yet, evidence is still lacking in larger, randomized studies.

Joshua W. Hustedt, MD, MHS
Department of Orthopedics
University of Arizona College of Medicine–Phoenix
755 East McDowell Road
Phoenix, AZ 85006
E-mail: joshua.hustedt@email.arizona.edu

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