



# Quadrimebral Amputation: A Review and Perspective on the Role of Composite Tissue Allotransplantation

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Quadrimebral amputees are those who have lost all or parts of both upper and lower extremities. There is a paucity of literature addressing the quadrimebral amputee and possible treatment options. We have reviewed the incidence, etiologies, and traditional treatment options for quadrimebral amputation. More recently hand transplantation, as a form of composite tissue allotransplantation, has become a new and viable treatment option for this subset of patients. A review of hand transplantation and outcomes is also presented.

## Introduction

By definition, quadrimebral amputees have lost all or part of both their upper and lower extremities. Compared to single limb amputees, they are more reliant on rehabilitation and prosthetics, yet with more modest expectations and outcomes. Despite carrying a rare diagnosis, quadrimebral amputees comprise a subgroup that can greatly benefit from continued medical innovation, not only in the form of prosthetics and rehabilitation, but more recently in the form of hand composite tissue allotransplantation (CTA).

## Incidence

Multiple limb amputations are very rare. Quadrimebral amputations are even more uncommon<sup>1</sup>. Canavese et al, in a retrospective reviewed of children with meningococemia over an 11 year period, found 48 patients with orthopaedic sequelae, 6 of which had quadrimebral limb loss defined as amputations above both the wrists and feet.<sup>2</sup> This may underlie the relative paucity of literature focusing on quadrimebral amputees.

## Etiology

Aside from congenital deficiencies, quadrimebral limb loss may occur secondary to a variety of etiologies such as trauma, sepsis, and vascular disease. Traumatic causes may include electrocution, motorcycle or severe vehicular accidents, and injuries such as falls under trains. Sepsis induced necrosis of extremities, especially from meningococemia in children, has also been reported<sup>3</sup>. At our institution, we have evaluated 5 quadrimebral amputees for enrollment in our hand transplantation program, all suffered necrosis in all four extremities secondary to pressor-induced ischemia or sepsis.

Both the social and personal costs of quadrimebral amputation are significant. In a study of multiple limb amputees only one-third of these patients were able to return to work<sup>1</sup>.

This is in comparison to a 63% return to work rate in the overall amputee population<sup>2</sup>.

## Literature Review

Garrison and Merritt demonstrated the potential for significant functional benefit from inpatient rehabilitation for quadruple amputees with end stage renal disease<sup>3</sup>. Three quadrimebral amputees, all with some degree of prior prosthetic fitting and a mean Functional Independence Measurement (FIM) score of 52 were admitted to inpatient rehabilitation. Median length of stay was for 24.5 days. Without any further prosthetic fitting, they were discharged with a markedly improved mean FIM of 75. Upon discharge, all three patients were able to perform sliding board transfers and using wheelchairs with assistance.

Celikoz et al. reported a case of a 25-year-old patient who sustained severe electrical burns after coming in contact with a high voltage power line<sup>4</sup>. This patient eventually required bilateral glenohumeral and bilateral below the knee amputations. At three month follow up, he was reported to have been fitted with myoelectric upper limb prostheses and bilateral leg prostheses, yet no long-term rehabilitation data was provided.

Kitowski has reported on two separate quadrimebral amputees involved in electrical burns<sup>5-6</sup>. The first patient is a 26-year-old man with bilateral below the knee and bilateral below the elbow amputations. After post-operative recovery he was fitted with bilateral upper and lower extremity prostheses and admitted for intensive rehabilitation. At discharge, he was efficient with activities of daily living including combing his hair, brushing his teeth, shaving and eating. Upon follow-up, he was able to drive and write legibly. The second patient is was a 21-year-old man who sustained severe burns when his oilrig came in contact with high voltage electrical lines. He required left above knee and above elbow, and right below knee and below elbow amputations. Through prosthetic fitting,

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rehabilitation and reconstructive surgery, he was able to attain independence in activities of daily living, including self-care, eating and ambulation, as well as driving a car. Substantial recovery of function, such as in these cases, is rare in the literature but does denote the potential for significant gains offered to quadrimembral amputees via the combination of intensive rehabilitation and prosthetic fitting in conjunction with the motivated patient.

Allport et al. conducted a study of 9 children who suffered from meningococcal septicemia necessitating limb amputation<sup>7</sup>. Five multiple amputees, either triple or quadruple, were included. Upon follow up, all patients were living in the community with minimal assistance. Functional assessment scores were low compared to age matched controls, yet organization and trouble shooting skills were normal with the exception of one child with cerebral involvement.

Davidson et al. described the case of a 38-year-old with bilateral transfemoral and transhumeral amputations secondary to a hang-gliding accident<sup>8</sup>. His 12-month rehabilitation, including prosthetic fitting, resulted in partial independence in activities of daily living. He was eventually able to walk, but still with a functional need for a motorized wheelchair. Davidson emphasized that although returning to work and leading a fulfilling life are possible, expectations should be realistic when full independence is not attainable.

Quadrimembral amputees face added challenges in comparison to those who have lost one or even two limbs. Those with bilateral transfemoral amputations may suffer from a loss of balance in sitting and rolling. They will also lack the propulsive and proprioceptive support used in ambulation. Bilateral upper extremity amputees lose the ability to interact with their surroundings and to maneuver objects in their environments, such as needed for activities of daily living and working. The significant loss of body surface area causes increased sweating, which may interfere with prosthetic fitting and utilization. Moreover, the energy expenditure needed for mobilization and ambulation may be substantially increased for multiple amputees. The combination of these impairments is perhaps not summated but exponential in its detrimental impact on the patient, the patient's disability and eventual rehabilitative potential.

### **Composite Tissue Allotransplantation**

Composite tissue allotransplantation (CTA), specifically that of hands and upper extremities may be an alternative to the traditional upper extremity prosthetic and rehabilitative treatment regimen for quadrimembral amputees. Combining microsurgery with the pharmaceutical advancements of immunosuppression, CTA has made transplantation of donor hands a reality<sup>9</sup>.

The indications for hand transplantation may include traumatic amputation, burn victims and ischemic induced extremity necrosis. Determining a patient's suitability for transplantation is paramount. Stringent evaluation of the patient's psycho-social support systems is needed to assess

their willingness to partake in long term physical therapy, endure the side effects of immunosuppression and weather the emotional challenges of organ transplantation<sup>10</sup>.

### ***International Registry on Hand and Composite Tissue Transplantation***

The IRHCTT reviewed hand transplants performed over an 11-year period (September 1998 - July 2010) and reported on outcomes<sup>11</sup>. They accounted for 49 transplanted hands, 17 unilateral and 16 bilateral. Due to an inability to obtain complete patient information, a subset of transplants in China and a few other centers were not included. We believe that to the total number of hands transplanted to this date may be well over 60 worldwide (IRHCTT and handtransplant.com)<sup>12-15</sup>.

In its most recent review, the IRHCTT reported one patient death (combined hand and face transplant) on day 65 from sepsis. Of patients transplanted in Western countries, 3 grafts have been lost. These included a right hand of a bilateral transplant recipient as a result of bacterial infection, a single hand from noncompliance, and a single hand from intimal hyperplasia and possible chronic rejection. This excludes a subset of patients in China, where 7 grafts which were lost due to abstention from immunosuppressive therapy, long distance from transplantation center and unreported episodes of acute rejection<sup>11</sup>.

The IRHCTT reported that all patients developed protective sensibility, 90% developed tactile sensation, and 82.3% had discriminative sensibility. Recovery of intrinsic and extrinsic motor function allowed patients to perform most activities of daily living. Moreover, 75% of recipients reported an improvement in quality of life and many have returned to work. Side effects were related to immunosuppression and included opportunistic infections, metabolic disorders and malignancies (one case of post transplant lymphoproliferative disease and a case of basal cell carcinoma of the nose)<sup>11</sup>.

Longer-term outcomes have been reported by Breidenbach et al. on 2 patients with 8 and 6 year follow up<sup>14</sup>. In functional testing, they noted results superior to those expected with prosthesis, including Carroll<sup>15</sup> test scores of 77/99 and 55/99 in comparison to expected prosthetic scores of 20-30. Both patients returned to work and reported excellent quality of life. Complications included avascular necrosis of bilateral hips treated with arthroplasty, cytomegalovirus infection, and immunosuppression related diabetes.

### ***Prosthesis versus Transplantation***

The difference in functional outcomes of transplanted hands has not been directly compared to that of prosthetic equivalents. However, studies of major limb replantation in comparison to prosthetics have been conducted. Peacock and Tsai described a 12-year-old girl with bilateral traumatic proximal humeral amputations of which only one side could successfully be replanted<sup>16</sup>. The other arm was fitted with a body-powered prosthesis. The patient was found to favor the replanted limb for activities of daily living.

Graham et al. used the Carroll test<sup>15</sup> and a modified version without prehensile tasks to compare functional performance

between a group of 22 major upper extremity replants and an equally sized group of prosthetic utilizers<sup>17</sup>. A statistically higher proportion of the replant group achieved excellent and good scores. Better outcomes were also found in younger patients and more distal injuries. The authors concluded that replantation of the injured upper extremity leads to better outcomes as compared to amputation and prosthetic use.

## Conclusions

Numerous multi-limb and quadrimembral amputees have received hand transplants in the United States and internationally. Most recently, in September of 2010, a bilateral hand transplant was performed in a 27-year-old quadrimembral amputee at the University of Pittsburgh<sup>13</sup>. She had lost her legs and parts of her hands after suffering a stomach virus 6 years prior. At the University Of Pennsylvania, our hand transplant program has listed 2 quadrimembral amputees and focuses on patients with multiple limb loss.

Traditionally, rehabilitation and prosthetic fitting has been the mainstay of treatment for patients with multiple amputations. Now, hand and upper extremity transplantation, as an innovative and life changing therapeutic, may also be considered in our armamentarium for the treatment of quadrimembral amputees.

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