Rehabilitation following hand transplantation

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Abstract

Background Hand allotransplantation can restore motor, sensory and cosmetic functions to upper extremity amputees. Over 70 hand transplant operations have been performed worldwide, but there is little published regarding post-hand transplant rehabilitation.

Methods The Brigham and Women's Hospital (BWH) Hand Transplantation Team's post-hand transplant rehabilitation protocol is presented here. The protocol must be modified to address each transplant recipient's unique needs. It builds on universally used modalities of hand rehabilitation such as splinting, edema and scar management, range of motion exercises, activities of daily living training, electrical stimulation, cognitive training and strengthening.

Results The BWH hand transplant rehabilitation protocol consists of four phases with distinct goals, frequency, and modalities. (1) Pre-operative: functional assessments are completed and goals and expectations of transplantation are established. (2) Initial post-operative (post-operative weeks 1–2): hand protection, minimization of swelling, education, and discharge. (3) Intermediate (post-operative weeks 2–8): therapy aims to prevent and/or decrease scar adhesion, increase tensile strength, flexibility and function, and prevent joint contractures. (4) Late (from 8 weeks forward): maximization of function and strength, and transition to routine activities. The frequency of rehabilitation therapy decreases gradually from the initial to late phases.

Conclusions Rehabilitation therapy after hand transplantation follows a progressive increase in activity in parallel with

wound healing and nerve regeneration. Careful documentation of progress and outcomes is essential to demonstrate the utility of interventions and to optimize therapy protocols.

Keywords Hand · Transplantation · Rehabilitation · Occupational therapy

Introduction

Hand allotransplantation (HA) can restore motor function, sensibility, and cosmesis to upper extremity amputees. After the first successful HA under modern immunosuppression [10], more than 50 patients have received transplants worldwide. Although much has been published regarding indications, surgical techniques, recovery and outcomes [25], there is little discussion of post-operative therapy protocols. Surgical technique and post-operative care of HA are akin to those of replantation, and thus many of the treatment and therapy protocols after HA are adapted from the replantation literature [18]. However, each HA recipient presents unique challenges to the rehabilitation team. Multiple factors such as the level and cause for amputation, age, comorbidities and immunosuppressive medications (which may affect stamina and well being) may affect the therapy plan and, ultimately, functional outcomes. Functional recovery following HA is a prolonged process with continuing improvements years after surgery and the rehabilitation professional must help hand transplant recipients during this prolonged period and continuously evolve treatment protocols [5, 20].

Return of motor and sensory functions after HA depends on transplantation level, healing and nerve regeneration, and may take months to years. Extrinsic motor function may never be lost when extrinsic muscles are native to the recipient and the majority of motion is simply transferred through the "pulley system" of allotransplanted tendons. Alternatively, return of intrinsic motor function is dependent on reinnervation of donor muscles

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and delayed innervation portends a worse prognosis. There are reports of intrinsic function by 9 months with neurovegetative function at 12 months after HA at the forearm level [10], and return to work (RTW) as a driver 2 years after transhumeral HA [8]. The timing of sensory function return is far more variable, and improvements continue years post-operatively [8, 10, 23–25]. Decreased sensation, neuropathic pain and cold intolerance are well documented and relate to sensory neural loss [33]. Lastly, some upper extremity amputees lack cortical representation and proprioception of the missing hand(s) due to prolonged time elapsed since the amputation(s). Cortical re-integration of the transplanted hand(s) is crucial to successful functional outcomes [3, 4, 10, 23].

HA can provide select recipients with sensate upper extremities able to perform tasks that may be impossible with prostheses [10, 23, 30]. The more distal the level of the transplant, the faster the functional recovery. Within a year after mid-forearm transplantation, many recipients function at a level equivalent to that with prostheses in activities of daily life (ADLs), with continuing improvements thereafter. Unilateral hand recipients may RTW sooner than bilateral ones. Due to the lack of data on hand therapy following HA, we wish to propose our protocol and use it as a starting point for future rehabilitation research in this field.

The BWH Therapy Protocol

The Brigham and Women's Hospital (BWH) generalized rehabilitation protocol for recipients of HA provides a solid foundation upon which modifications are made to address each recipient's specific needs. The protocol was developed for recipients of mid-forearm transplantation, but can be adapted to other levels of transplantation. The protocol is approved by the Partners Human Research Committee (Protocol 2012P000073); all subjects who enroll in this study provide informed consent. The following therapy modalities are employed (Fig. 1):

- Splinting — to help protect the repair of the tissues and coaptation of tendons by keeping insensate and weak transplanted hands in positions optimal for healing, and to provide a basis for avoidance of joint contractures [13].
- Edema and scar management — to prevent inhibition of motion and adhesions. Static compression is the mainstay of edema and scar control. Massage and motion is typically used to ameliorate scarring.
- Range of motion (ROM) exercises — to avoid tendon and joint adhesions and maintain gliding mechanisms, which are critical at the time of motor function return.
- ADLs — to train the recipient to perform many complex tasks required of the hands, by integrating the brain,

peripheral nerves, muscles, tendons, and joints to use the transplanted hand(s).

- Electrical stimulation — for pain control, reduction of edema, muscle strengthening and wound healing [2]. Although the evidence regarding its utility is controversial, we believe that it may help with maintenance of neuromuscular junctions and muscle hypertrophy, as well as an adjunct to passive ROM — acting as a pseudo-active ROM — while muscles regain strength and/or innervation [29].
- Cognitive training — to help augment the re-learning of the cortical map of the hands in the brain. The ability of the brain to sense and power a newly transplanted hand is clearly important to ultimate function.
- Strengthening — as bony and tendinous junctures heal, the opportunity to strengthen muscles powering the hands increases, further broadening the functions possible for hand transplant recipients.

The therapy protocol is divided four phases, each with specific goals:

- Pre-operative phase with goals to inform/educate the patient, assess, make recommendations, and provide preparatory treatment.
- Initial phase (post-operative days 0 to 14) with goals to protect the transplanted hand(s), minimize swelling, provide education and plan discharge.
- Intermediate phase (3 to 8 weeks) with goals to prevent and/or decrease scar adhesion, increase tensile strength of tissues, flexibility and function as well as prevent joint contractures.
- Late phase (8 weeks onwards) with goals to maximize function, increase strength, monitor sensory recovery, and transition to routine activities.

Pre-operative Phase

Pre-operative evaluation may take place months before the transplant operation and may include multiple visits. During this phase, we collect information such as medical history, injury history, previous treatment(s), and occupation. We perform integumentary analysis and assessments of stump size, shape, length, sensitivity and baseline pain, ROM, strength, sensory status of both upper extremities from shoulders to digits, functional analyses, and ability to perform ADLs. We also evaluate the patient/family's ability to understand, cope with and follow through with treatment, and we develop fundamental and reasonable functional goals. We use standardized documentation and testing.

Lastly, we develop a plan of care that addresses factors that may compromise a successful outcome, for example, proximal upper extremity and/or trunk weakness. For those considering bilateral HA, we discuss with the patient and family that

HAND TRANSPLANT THERAPY PROTOCOL OVERVIEW (Initial 6 Months)																
	Day							Week			Month					
	1	2	3	4	5	6	7	2	3	4	2	3	4	5	6	
Splinting	Dynamic crane extension outrigger splint									Anticlaw splint	Dynamic splint			Discontinue splint		
Range of Motion	None	Early protected motion						Wrist PROM, tenodesis, place and hold	Wrist AROM, tenodesis	F/arm supination & pronation, composite ROM & blocking exercises			Unrestricted ROM			
Electrostimulation	None							EMS of wrist and finger flexors and extensors				EMS of intrinsic				
Cognitive Training	None							Neurocognitive rehabilitation (Perfetti)								
ADLs	None	Basic one-handed ADLs						One-handed ADLs, 3-point pinch			Two-handed ADLs			Return to work		
Edema/Scar Management	Daily xeroform/DSD dressing change							Light compression wrap, positioning		Compression garment, scar massage						
Strengthening	None									Light resist activities	Basic strengthening exercises					
Testing	None										6 weeks		12 weeks		24 weeks	
Setting	Inpatient							Outpatient								
Schedule	None	6-7 hours daily, 5 days per week (BWH)									4-5 hours daily, 3 days per week (home site)					

Fig. 1 Brigham and Women's Hospital rehabilitation schedule for the first 6 months following HA

initially after the surgery, there will be complete dependence on caregivers.

Initial Phase (Days 0 to 14)

Immediately after HA, all therapy takes place in the in-patient setting. In-patient length of stay is typically 1–2 weeks, barring complications. The transplanted limb(s) is/are dressed, the choice of which is dependent on the quality of the skin, edema, vascular stability, and need for monitoring. We typically use a thermoplast volar resting orthosis fabricated pre-operatively, that helps keep the hand in a resting position while preventing joint contractures. Therapy takes place daily, with sessions spread throughout the day and active participation by rehabilitation professionals, nursing staff, and the hand transplant recipient's family. Collaboration between nursing, surgical and therapy groups is important for dressing and monitoring wound and soft tissue status. Nurses provide 24-h monitoring and help carry out the ROM program. Wound care is performed in a warm environment to avoid vasoconstriction. Recipients are educated about positive and negative factors affecting wound healing. Edema is managed through positioning and later through compression. The transplanted hand(s) are positioned to avoid vascular compromise and edema, protect the repairs, and ensure optimum length–tension relationships between extensor and flexor tendons [26]. A dynamic crane extension outrigger orthosis (Fig. 2) is fabricated as soon as possible after surgery, and the hand transplant recipient wears it continuously during the day. A night forearm intrinsic plus orthosis is used because hand transplant recipients are very prone to the intrinsic minus position due to lack of ulnar nerve function during recovery.

We introduce passive ROM exercises within the first 1–3 days post-operative, and evaluate perfusion on every digit before treatment. If the hand transplant recipient's native extrinsic flexor and extensor muscles are present and functioning, we start early active motion (EAM) of the metacarpophalangeal (MP) and interphalangeal (IP) joints with emphasis on assisted motion within the confines of the dynamic crane orthosis by the end of post-operative week 1. Active tension at tendon repair sites is recommended to allow proximal movement that may not happen with passive motion alone [11]. Physical therapy for out-of-bed activities starts in week 2, especially important in hand transplant recipients who also have lower extremity amputations and use prostheses.

Intermediate Phase (3 to 8 Weeks)

Hand transplant recipients are discharged from the hospital within this phase and transition to out-patient rehabilitation, 5 days per week, 4–6 h/day. By week 5, we decrease this frequency to 4–5 h/day, 3 days per week. We encourage hand transplant recipients and their families to remain engaged with treatment; they are responsible for weekend treatment themselves.

We utilize the crane orthosis throughout the intermediate therapy phase. We introduce a dorsal blocking or anti-claw orthosis with added thumb opposition on post-operative week 4 (Fig. 2), and use it for as long as needed to prevent clawing, substituting for non-innervated intrinsic muscles. We institute dynamic, static, and static–progressive orthosis as needed to prevent contracture, minimize muscle imbalances, and protect and position the hand(s) for function. We perform daily scar and edema management using compression (i.e., Coban™, Tubigrip™, Kinesio® tape and gloves), mobilization,

Fig. 2 Types of orthosis (splints) used as part of the Brigham and Women's Hospital HA rehabilitation protocol. The dynamic outrigger orthosis is implemented as soon as possible after surgery for continuous use during the day. The dorsal blocking orthosis is introduced on post-operative week 4, and used for as long as needed to prevent clawing

elevation, and massage. As tissues mature, we increase the intensity of compression [29].

Once bony healing is evident, we begin gentle tenodesis exercises, consisting of gentle wrist flexion and simultaneous finger extension, followed by bringing the wrist to about 15–20° of extension, with gentle active and active-assisted flexion of the digits. The motion of wrist and MP joints must be proportional in order not to stress any tissue and to maintain the length/tension ratio between flexors and extensors.

Early in the intermediate therapy phase, we introduce 3-point pinch and bilateral hand usage, such as picking up pieces of food, stacking blocks, and transferring items from one hand to the other. If the transplant is unilateral, the hand transplant recipient can assist with donning and taking off the orthosis as well as performing more involved self-care tasks. We initiate ROM of shoulder and elbow and ADLs by the beginning of week 3. We start with basic light ADLs (such as hand-to-mouth for self feeding) with assistance, and gradually progress. We introduce "place and hold" exercises at the end of week 3, and add active ROM of the wrist, active use of the hand for light activities and thumb opposition by week 4. In this stage it is important to pay attention to finger extension to prevent PIP flexion contractures. In week 5, we initiate gentle ROM exercises involving the forearm, such as supination and pronation and gentle blocking exercises of digits. Barring complications with wound healing, we implement unrestricted ROM in week 6. By week 8, we add two-handed ADLs (such as brushing teeth and toileting) as motor control and strength increase, and begin stretching of adhesions using moist heat [15]. If there is satisfactory active ROM, we initiate strengthening around week 8. We use various tools such as therapy putty, weights, wall pulley, ergometer, Thera-Bands®, hand exerciser and functional hand use. We monitor these exercises closely, to ensure appropriate pressure, proper positioning and to avoid injuring insensate hands.

As soon as we observe active motion of the digits, we incorporate cognitive therapeutic training, in order to help the hand transplant recipient form a mental picture of activities and have a reference for repetition. We base our approach on cognitive therapeutic exercises developed by Perfetti; asking hand

transplant recipients to make mental representations of the most accurate performance of tasks which increase in complexity and aim at motor recovery using proprioceptive feedback [32].

Lastly, we introduce electrical stimulation simultaneous to the start of active ROM of the wrist. We use two types of electrical stimulation: transcutaneous electrical nerve stimulation (TENS) and neuromuscular electrical stimulation (NMES). TENS helps with pain control and NMES with muscle re-education. We use high and low rate stimulation for sensory and motor goals, respectively [29]. TENS is applied as needed for management of pain; we use frequencies >50 Hz for 20–30 min while performing ROM exercises. The intensity is high enough to block the pain but should be comfortable and not produce contraction. NEMS is used for muscle re-education. We use 35–50 pps, 300 width, 3–5 s ramp and a 4:12 on/off duty. The intensity is enough to produce contraction yet still be comfortable. We also provide a unit to the hand transplant recipient with instructions for use at home.

Late Phase (Week 9 Onwards)

In this phase, we further reduce treatment frequency to 4 h/day, 3 days per week; although recipients continue daily therapy at home alone and with family. We do progressive work with ADLs, function of the transplanted hand(s), and reintroduction of prior activities. After week 12, hand transplant recipients who live away from the treatment center may return home and continue treatment there. By week 24, we further reduce the schedule to 4 h, twice per week. The hand transplant recipient can work to gradually return to his/her prior routine during the next 24 weeks and may be able to RTW. We recommend yearly reassessment at the transplant center.

Testing

We administer formal testing including self-report and quantitative measures at baseline, 6, 12 and 24 weeks post-transplant and every 6 months thereafter, as follows:

1. Standardized score systems:
 - (a) Disability of the Arm, Shoulder and Hand (DASH) Questionnaire [16], an evaluative outcome measure that is a self-administered questionnaire on symptoms and functional status.
 - (b) Hand Transplantation Score System [19], a specific functional score developed by the International Registry of Hand and Composite Tissue Transplantation.
 - (c) Short Form 36 (SF-36), a generic survey to measure functional health and well-being [33].
 - (d) EQ-5D, a standardized, simple instrument that provides a single index value for health outcome [14].
 - (e) Global function testing: We use the Carroll test, which evaluates global functional capabilities in everyday use with a 0–99 point scale, assuming that everyday use of the upper extremity can be reduced to certain patterns of movement [6].
2. Nerve regeneration testing: We monitor Tinel signs, which involves applying percussion over the level of the regenerating nerve which will produce "pins and needles" distally in the distribution of that nerve [31].
3. Sensibility testing: We use Semmes–Weinstein monofilament test for detection of a single stimulus (described by Feng et al. [12]), Dellon's moving two-point test for discrimination [9], and the modified Moberg test [21] to demonstrate recognition.
4. Strength: We measure the amount of force a muscle can sustain using the Jamar hydraulic dynamometer and the pinchometer [29].
5. Flexibility: We record ROM using standard techniques with a goniometer [29].
6. Pain: Measured using the Visual Analog Scale (VAS) [17].
7. ADLs: This consists of observing the hand transplant recipients as they perform various ADLs such as eating, drinking, or buttoning a jacket.
8. Dexterity: We use the 9-Hole Peg Test, where patients have to pick up pegs one at a time, put them in the holes and then remove them again one at a time. We record the total time to complete the task [22].

We document many of these assessments in video format to allow for later review and to demonstrate functional outcomes that cannot be easily documented by numerical metrics.

Discussion

Setting and Schedule

The setting for rehabilitation following HA depends on an individual's needs and available facilities. In our program, we attempt to discharge hand transplant recipients as soon as practical, provided there is systemic stability, pain control,

stable immunosuppression, and appropriate home support. Typically, we aim for postoperative week 2. We actively encourage hand transplant recipients and their families to participate in therapy, and expect them to continue daily therapy even when at home. The frequency, modalities and intensity of our rehabilitation protocol appears in line with those published by others [10, 24, 27]. The frequency and intensity of rehabilitation therapy may be easily overestimated; gradual tapering in both frequency and intensity would allow the recipients to regain a sense of control over their time and minimize fatigue.

Testing and Documentation

As with any new procedure or intervention, testing and documentation are key to refining and improving. The ability to accurately record our outcomes will allow us to compare results and objectively critique our hand transplant recipient selection criteria, operative variables, and rehabilitation protocols. Many of us expect HA to become a standard of care for limb amputees. However, evidence of improved outcomes over the existing alternatives (no surgery, prostheses, etc.) is required in order to provide unbiased informed consent to patients and to expect third parties to cover the associated costs. At this stage, our measurements remain fairly rudimentary, consisting of scales evaluating primary outcomes (such as joint ROM) and secondary outcomes (such as ability to perform certain tasks). Overall function is harder to measure and is often best captured when speaking with hand transplant recipients and videoing their day-to-day activities. Our various scoring systems focus on different aspects of recovery and function. It is likely that over the next years these scoring systems will be further refined and our abilities to measure and assess outcomes will improve.

Cost

Although rehabilitation is essential for recovery of function after hand transplantation, a rehabilitation protocol such as the one described here is significantly expensive and this may constitute a prohibitive factor for patients and institutions. Costs could be reduced in the future by developing and incorporating elements of automated rehabilitation through the use of tablets, videogames and other electronics. In addition, the recipient and his/her family members can be educated to support as much in-home, "self-administered" rehabilitation as possible, especially in unilateral hand transplant recipients. Lastly, cost reduction could also be accomplished through an "economy of scale" approach, where centers performing multiple HAs per year could hire a full-time certified hand therapist to provide all rehabilitative services.

Patient Motivation

Rehabilitation after transplantation can seem lengthy and slow to patients, families, and therapists. Typically, there is rapid improvement in the initial weeks with the sudden presence of a limb that was previously absent. However, it is difficult to prepare any patient for the many months necessary for neuromuscular connections that lead to developing distal sensation and intrinsic muscle function. Patient selection is perhaps the most important predictor of success in this area. Numerous groups have found that patients who anatomically and physiologically appear to be ideal surgical candidates have had less-than-optimal outcomes due to a waning of participation in therapy during the months and years that follow HA. While it is hard to objectively study, we believe that a strong family support mechanism, good pre-morbid functioning, and a tight relationship with the surgical and therapy teams are critical for success.

Unique Challenges: Multiple Amputees, Blindness, and Others

It is not uncommon for upper extremity amputees to have multiple additional disabilities. We commonly evaluate patients with associated lower extremity amputations, associated traumatic disabilities (such as facial injuries and blindness), and multiple medical co-morbidities. These additional disabilities may make rehabilitation significantly more challenging. Patients with lower extremity amputations will require additional physical therapy, additional time to return to walking independently, assistance while returning to walking without the ability to weight-bear on upper extremities, and more inpatient and/or rehabilitation facility care. Avoidance of pressure ulcers is critical in this patient group.

Transplantation in the blind has been a controversial topic. We recently published on this topic [7], and feel that blind patients stand to gain significantly from the transplantation of a sensate hand. Their rehabilitation is, clearly, more complex — depending on non-visual cues such as proprioception for feedback.

A set of broad guidelines was developed by the American Society for Reconstructive Transplantation which broadly outlines indications and contraindications [1].

Conclusions

Hand transplantation is rapidly gaining acceptance by patients, physicians, and rehabilitation professionals. Peri-operative therapy is based on our prior experience with replantation patients, and follows a progressive increase in activity in parallel with wound healing and nerve regeneration. Careful record-keeping and documentation of progress and outcomes is essential in order to demonstrate the utility of this intervention and better tailor and improve our therapy protocols.

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Statement of informed consent Informed consent was obtained from all participants and all procedures were conducted according to the Declaration of Helsinki. The authors of this manuscript state that all procedures followed in the studies described here were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2000 and 2008. The Hand Transplantation study at Brigham and Women's Hospital, inclusive of the herein described rehabilitation protocol, is approved by the Partners Human Research Committee (Protocol 2012P000073).

Conflict of interest The authors have no financial disclosures. None of the authors has a financial interest in any of the products, devices, or drugs mentioned in this manuscript.

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