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Muhammad Ahsan Ali, Year 6, Group 7

INTEGRATED STUDY MASTER'S FINAL THESIS

Rankos alotransplantacija prieš modernų rankos protezą: istorija, indikacijos, privalumai ir trūkumai, ateities perspektyvos. Literatūros apžvalga.

Allotransplantation of the Hand vs Modern Hand Prosthesis: History, Indications, Pros and Cons, Future Perspectives. Literature Review

Supervisor Assistant professor Dr. Nerijus Jakutis

Head of the clinic Professor Irena Butrimienė, PhD

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Student's email address Ahsan.ali@mf.stud.vu.lt

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1.Abbreviations

RPHs- Robotic Prosthetic Hands

CTA- Composite Tissue Allotransplantation

VCA-Vascularized Composite Allotransplantation

3DP-3-Dimensional Printing

ARAT- Action Research Arm Test

SHAP- Southampton Hand Assessment Procedure

DASH-Disabilities of Arm, Shoulder, and Hand measure

SF-36- Short Form-36

2. Santrauka

Šiame darbe nagrinėjami įvairūs rankos alotransplantacijos ir šiuolaikinių rankų protezų aspektai, ypatingą dėmesį skiriant jų taikymo indikacijoms. Indikacijos buvo analizuojamos remiantis apklausa, atlikta bendradarbiaujant su American Society for Surgery of the Hand. Darbe aptariami svarbiausi rankos alotransplantacijos privalumai, tokie kaip sensorinių ir motorinių funkcijų atkūrimas, tačiau taip pat pabrėžiama, kad šiam rezultatui pasiekti reikalinga ilga ir sudėtinga reabilitacija, kuri laikoma vienu iš pagrindinių šios procedūros trūkumų.

Lyginant su rankos alotransplantacija, rankos protezai yra ekonomiškesnis sprendimas, tačiau jie taip pat turi tam tikrų ribotumų, kadangi negali visiškai atkurti sensorinių ir motorinių funkcijų. Ateities perspektyvoje rankos alotransplantacija išliks reta procedūra dėl itin aukšto chirurginio meistriškumo, sudėtingų mikrochirurginių technikų bei didelių finansinių išlaidų, susijusių su specializuota įranga ir procedūros tikslumu. Tuo tarpu sparčiai vystomos robotizuotos ir bioninės rankos, kurių pagrindinis tikslas – kuo tiksliau atkartoti natūralios žmogaus rankos funkcijas.

Darbe taip pat atliktas 3D spausdintų ir komerciškai prieinamų protezų palyginimas, vertinant skirtingų tipų suėmimus bei rezultatus pagal „Anthropomorphism Hand Assessment Protocol“. Tyrimo rezultatai parodė, kad komerciškai prieinami protezai pasiekė geresnius vertinimo rezultatus. Be to, buvo lyginami rankos protezų ir rankos alotransplantacijos funkciniai bei

psichosocialiniai rezultatai. Reikšmingų skirtumų funkciniuose rezultatuose nenustatyta, tačiau pacientai po rankos alotransplantacijos pasižymėjo geresniais psichosocialiniais rodikliais.

3. Summary

This thesis has looked upon various aspects of hand allotransplantation and modern hand prosthesis in terms of their indication which are explained further using a survey done with American Society for Surgery of the Hand. Moreover, it also shines light upon some the most important advantages of hand allotransplantation such as full restoration of sensory and motor functions; while also highlighting the fact it needs a long rehabilitation to achieve, which counts as a drawback for it. Hand prostheses are cheap as compared to allotransplantation, but they bring their set of challenges such as no restoration at all sensory and motor function. From a future perspective hand allotransplantation will be a relatively rare procedure due to immense skill level needed and microsurgical techniques required, making it an expensive procedure due to usage of high quality of instruments and precision required, whereas work on rapid basis is being done to make prosthetic arm robotic, moreover rapid work is being done on bionic arms which had a main aim of mimicking a natural hand. A comparison was done to evaluate which types of prosthetics have advantage 3D-printed one or commercially available prosthesis in terms of different types of grips and maintained score evaluated by Anthropomorphism Hand Assessment Protocol which clearly showed commercially available prosthesis as clear favorites in terms of the test. Another comparison between prosthesis and hand allotransplantation was done to see functional and psychosocial outcomes , there were no significant difference in the functional outcomes of both prosthesis and hand allotransplantation , although patients with hand allotransplantation scored more at psychosocial outcomes.

4. Keywords

Hand Allotransplantation , Hand Prosthesis , Below-Elbow Amputees , Robotic Hand ,Indications of Transplantation, Bionic Arms .

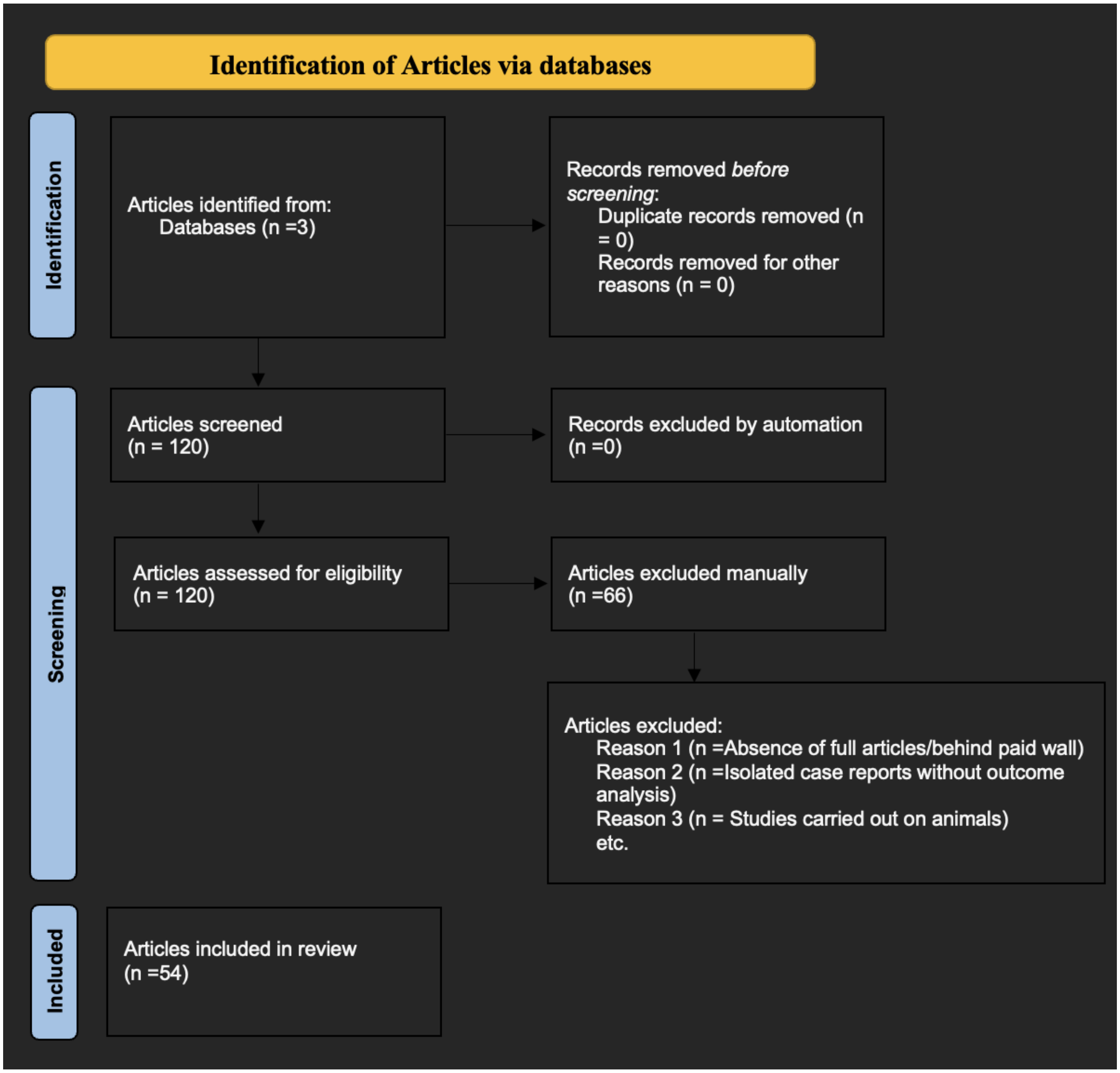
5. Introduction

The human hand is a complex biological structure that enables individuals to execute various actions, encompassing both precise and forceful movements. As a result, the loss of an upper limb can impede a person's capacity to manage daily tasks. Furthermore, it may precipitate a variety of emotional and psychological issues, such as anxiety, depression, and post-traumatic stress disorder(1). Even though there might be a certain degree of unreliability in long-term predictions, it is predicted that the numbers correlating with loss of the upper limb will continue to expand, with an estimated 540,000 patients currently in the United States of America and a yearly addition of 30,000 cases(2)(3). Data from a nationwide study conducted in Germany from 2019-2023 revealed 5,427 cases in 2023 , which shows a slight decrease of 7.3% since 2019(4), even if total incidence of upper limb loss is decreasing, the etiology of upper limb loss is shifting towards medical causes which supports the prediction of future increase with no rough estimation provided in the study but increase in these cases might be due to aging, diabetes epidemic and vascular disease. There are two schools of thought depending on the situation, one thought backing Allotransplantation, while the other is in favor of RPHs depending on the situation. Despite countless attempts and centuries of work towards making artificial hands prosthetic and providing them with the same biological features, today we have new RPHs, which are close to biological hands. This review will evaluate different types of RPHs in comparison to allotransplantation of a hand to establish which is overall effective based on existing literature. Furthermore, in this review, we will highlight the benefits and drawbacks of the most popular RPHs compared with allotransplantation of the hand.

6. Literature Search

Literature search was performed with the already mentioned keywords using PubMed, ScienceDirect, and Web of Science. The inclusion criteria of articles were only original articles written in English, then full texts of relevant articles were extracted after being screened for titles and abstracts. Moreover, articles written by original authors were selected. Exclusion criteria included the absence of full articles and those behind paywalls; moreover, isolated case reports without outcome analysis and studies carried out on animals were excluded.

Figure 1:PRISMA Flow Diagram of Articles



7. Historical Development

7.1 Evolution of Hand Allotransplantation

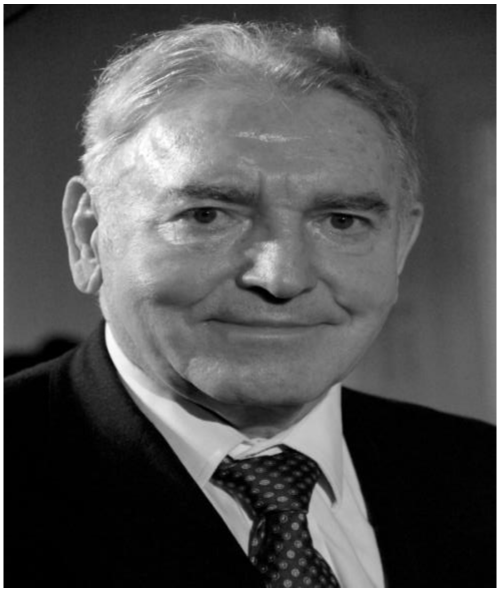
To begin with hand allotransplantation, one must familiarize themselves with CTA also known as Vascularized Composite Allotransplantation(VCA) in today's modern world. VCA are grafts that are made up of multiple different tissues but are transplanted all together as a single unit. One of the most typical example is of hand graft that is prepared for transplantation, which consist of muscle, skin , bone, and nerves. Due to these attributes CTA differs from solid organ transplantation as it aims primary to enhance functional ability and physical appearance rather than to ensure survival(5).There are 4 most common forms of CTA which include hand transplantation , face transplantation, abdominal wall transplantation and laryngeal transplantation. The most widely performed and studied form of CTA are upper limb(hand) and face transplantation, both of which have shown the ability to restore significant levels of function and improve patients quality of life(6). Moreover other procedures such as abdominal wall and laryngeal transplantation further show the expanding reconstructive role of CTA in complex tissue defects(7). Face transplantation and bilateral hand transplantation are regarded as most advanced type of CTA , since they require careful incorporation of various types of tissues , the recovery of motor and sensory activity and dealing with serious immunological issues, specifically , joint surgeries (e.g. simultaneous face and hand transplantation) are the most complex surgical and multidisciplinary procedures(8). More recently, the area of CTA has grown to include new and emerging uses , including uterus and penile transplantation , as a preference to procedures that focus on quality of life and functional restoration over traditional reconstruction(9). Moreover they are exploring new tissue engineering and immunomodulatory approaches to avoid the necessity of immunosuppression on a lifelong basis and increase positive outcomes ultimately(9). Altogether, CTA is one of the most quickly developing areas of research related to transplantation and reconstructive surgery that gives promising solutions to the patients with the complicated loss of tissues and makes it a serious clinical/ethical issue.

Hand transplantation is a surgical procedure that has evolved over time through close collaboration between reconstructive and transplant surgeons (10). Technically, the procedure is similar to hand replantation (11), which is the surgical reattachment of the patient’s own amputated hand after traumatic amputation. Unlike other single-organ transplants, hand transplants are a CTA which compromises of skin, muscle, tendons, bone, cartilage, fat, nerves, and blood vessels. While the skin acts as a primary barrier and a specialized immunological network, it possesses the highest scope for antigen recognition among all human tissues(12), which induces an intense adaptive response due to recognition of foreign antigens.

The first attempted hand transplant took place in Ecuador in 1964 (11). During these initial times, immunosuppressive treatments were at its infancy, so a regimen of prednisone and azathioprine was insufficient to prevent irreversible acute rejection within two weeks of the transplant. At that time, leaders in transplant surgery believed that it was impossible to successfully control or overcome the immune rejection associated with CTA. The following three decades saw major advances in solid organ transplantation(11).

By the 1980s, they successfully demonstrated long-term survival of limb transplantation using low-dose cyclosporine(13). In September 1998, the first human transplant was performed by a team of surgeons in Lyons, France(14). This evolutionary transplant was led by Jean-Michel Dubernard (1941-2021), who transplanted the right forearm of a brain-dead donor to a male recipient (Clint Hallam) aged 48 with a traumatic midforearm amputation(14). The procedure lasted over 13 hours; its initial success was only short-lived, as the patient could not cope psychologically with the integration of an unfamiliar hand, furthermore, resulting in the patient not following his post-operative immunosuppressive regimen, which resulted in acute tissue rejection. The initial transplant of a first human hand indicated a few significant lessons to be considered when developing a composite tissue allotransplantation, it is quite evident that technical success is not enough and that long terms results are dependent on the psychological acceptance of the graft by the patient. So, this case highlighted the fact how important the patient choice with , in detail psychological screening is and how vital it is to follow the lifelong immunosuppressive regimen in averting rejection. Moreover , it also highlighted the importance of multidisciplinary response that would be required from surgical , psychological and rehabilitative care that will lead to successful outcomes of CTA.

Figure 2: Jean-Michel Dubernard



Finally, on January 24-25, 1999 first successful long-term hand transplant took place in Louisville, Kentucky(USA). The pivotal efforts of this team provided the foundation for the subsequent triumphs of hand transplant units globally. Whereas progress in the field of CTA had previously been sluggish, the field began to witness rapid advancements.

The first ever double transplant was performed in Lyons in 2000, as by then, manipulation of the immune response had become more refined using traditional immunosuppressants(15). This made way for other forms of CTAs to be used.

In 2002, Dubernard founded the International Registry on Hand and Composite Tissue Transplantation (IRHCTT), the main aim of which was to advance the science of CTA by combining clinical experience from around the world and making it easily accessible to transplant specialists in the international community(16).

7.2 Evolution of Hand Prostheses

Although the invention of artificial limbs has been centuries underway, it still needs a long time to come up with a device that closely resembles the biological limb. Additive manufacturing or 3DP of limbs began to influence the field of prosthetics in 2012 when the first-ever 3DP prosthesis named “Robohand” was introduced (17).A picture of “Robohand” can be seen in Figure 3. The technology has since been advancing at a quick pace and maturing, and more 3D-printed prosthetic devices have been made available. However, more work is still needed to enhance the anthropomorphism and cosmesis of 3D-printed prostheses, their comfort, durability, and functionality. Additionally, these prostheses are more often aimed at children, in large part because of their continual development, which implies a periodic change of prosthesis(18).

Figure 3: First ever 3DP protheses "Robohand"

8. Indications

8.1 Indications for Hand Allotransplantation

In CTA, which involves a surgical and immunologically invasive procedure with lifelong medications, hence the patient selection criteria are crucial for CTA. Keeping the principle of “Primum non nocere” as the foundation of medicine, which emphasizes that a surgical intervention is only indicated if a patient's life time can be prolonged, their condition can be improved, and additional risks are acceptable and outweighed(19). Based on current medical literature and international registers, there are no widely set or absolute indications for CTA, instead the contraindications are more easily defined. To begin with, the primary indication of hand allotransplantation is when loss of function severely limits daily life(20), even if the person still interacts socially, as this creates a spectrum between function and social identity, hence the primary indication is to restore function rather than appearance.

A web-based survey conducted by Mathes et al. regarding CTA was sent to the members of the American Society for Surgery of the Hand, which asked them about a series of issues, including the indications for hand allotransplantation. The results of indications for allotransplantation of the hand are depicted below in Table 1(21).

Table 1: Indications For Hand Transplantation

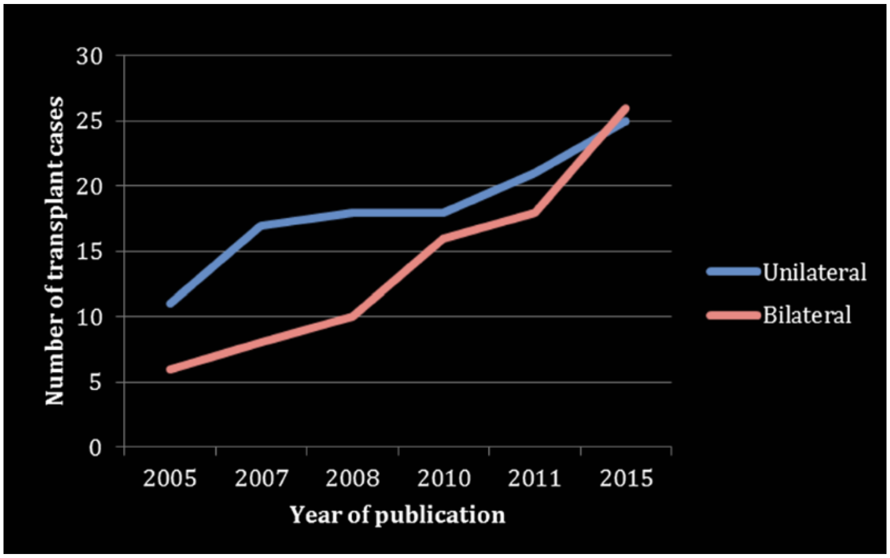
TABLE 3. Indications for Hand Transplantation

Indications for Hand, Partial Hand, or Digit Allotransplantation Should Include	Frequency	Percentage (%)
Amputation of bilateral hands	366	78%
Amputation of dominant hand	148	32%
Multiple failed reconstructions (e.g., failed toe to thumb)	127	27%
Amputation of thumb	92	20%
Amputation of multiple digits	79	17%
Amputation of non-dominant hand	65	14%
There is no acceptable indication for hand transplantation	81	17%

As per the results of the survey, it can be deduced that the most accepted indication for hand allotransplantation by the American Society for Surgery of the Hand is bilateral below-elbow amputation(78%). However, only 32% also supported the idea of hand transplantation in patients after unilateral amputation of the dominant hand. It can also be noted that the majority of surgeons were not in favor of transplantation of the non-dominant hand as an indication for hand transplantation. Moreover, 17% of the surgeons adopted the idea that there is not one or multiple indications for hand transplantation, rather it depends on every single individual case.

According to one of the reports from the International Registry on Hand and Composite Tissue Allotransplantation, 44% of the transplanted patients were bilateral amputees(19). This backs up the same idea of American society for hand surgeons, hence making bilateral amputees an absolute indication for hand allotransplantation. Moreover, in the same report, a review was published covering the worldwide experience of upper extremity transplantation; all cases were summarized via a line graph depicted in Figure 4(19).

Figure 4



This graph summarizes the relationship between unilateral and bilateral cases from the total number of hand transplants performed. It can be noted that over the past 10 years, there has been a clear rise in the number of transplant cases for bilateral amputees, overtaking unilateral amputations. There might be one limitation in this review, which can be the case that many unilateral amputations did not undergo transplantation, as the patient's autonomy preferred hand prostheses, or they had no clear match; it might be the case that many unilateral amputations go unrecorded. Extrapolating the trend, it is quite evident that bilateral amputations are an absolute indication for hand allotransplantation.

Moreover, in a survey, the American surgeons were also asked about the level of risk associated with hand transplantation. The results were noted as following presented in Table 2(21).

Table 2: Risk Associated With Hand Transplantation

TABLE 1. Level of Risk Associated With Hand Transplantation

What Level of Risk Do You Assess to a Hand Allotransplant?	Frequency	Percentage (%)
High risk	327	69%
Medium risk	114	24%
Low risk	8	2%
Cannot assess risk level	24	5%

It can be evaluated that many of the surgeons backed the idea that there is a high level of risk involved in hand allotransplantation(69%). This may be because in CTA, many complex elements are involved, which need to match for a successful transplant from tiny nerves to blood vessels and then skin, which has the highest scope for antigen recognition, making it highly risky to transplant a hand. There were also a small number of surgeons backing the thought that hand transplantation has a low risk(2%), whereas (5%) adopted the idea that the risk level cannot be assessed, as every case is different and should be dealt with accordingly.

So, overall, hand transplantation is indicated in a very small set of patients who have lost an upper limb or have a severely damaged arm that is functionally useless and standard treatments are not good enough, such as surgical reconstruction(Tendon transfers, bone reconstruction, skin flaps) or failure of modern hand prosthetics, which fail to restore acceptable function for daily life.

As per one article written by S.T. Hollenbeck(20), potential indicated populations of patients are mentioned for hand transplantation. Patients not requiring new immunosuppression (22), because CTA generally requires lifelong immunosuppression, so it is important to look for patients who would not need to start new immunosuppression. One of those categories of patients can be prior organ transplant recipients, as patients are already taking immunosuppressive drugs. This principle has already been applied in abdominal wall transplantation for patients receiving small bowel transplants from the same donor (20).

Another indication from the same categories as mentioned earlier can be congenital deformities, which are considered a potential indication (20). This is because severe congenital deformities may involve loss of multiple tissue components. This may be an indication for potential transplantation when conventional reconstruction and prosthetic options do not provide or restore the same adequate functional, sensory, or aesthetic restoration, and transplantation can significantly improve the life of the patient.

8.2 Indications for Hand Prosthesis

Indications for Hand Prosthesis are also not an absolute set of indications that can be used to rationalize the use of a prosthesis. One of the indications mentioned in most of the literature is that fitting of prosthetics would be normally practiced after 3 months of amputation to decrease muscle atrophy and assist in the restoration of normal functions. This emphasizes how the hand and prosthetic rehabilitation can be used during the acute period and not as a predictor of hand transplantation, which is normally used in patients who have major functional losses that are not covered sufficiently covered with the help of artificial hand.

Firstly, the extent of amputation matters as prostheses are indicated for both unilateral and bilateral amputations. It is seen in unilateral cases that patients often find they can cope effectively using one functional hand along with prosthetics, making them less willing to accept the medical risks associated with hand transplantation, such as lifelong immunosuppression(23).

The level of amputation also plays an important role in determining whether a prosthetic is the best for a patient. The typical levels of upper limb amputation include: transradial (below the elbow, forearm level) , transhumeral (above the elbow), and shoulder level amputations. The functional implication in each level is unique and will be examined such that it identifies the best indication of hand prosthesis.

<u>Below the elbow:</u> This level offers the best possible outcomes for prosthetic devices(24), however, the result of the prosthetic in daily life is strongly dependent on the shoulder and elbow function of the patient. A good shoulder and elbow joint is crucial to move the prosthetic device in three-dimensional space. The most used below-the-elbow prosthesis devices are myoelectric

prostheses, which are controlled by two individual groups of muscles of the remaining hand, making use of the signals from one muscle group to open and another to close the hand, and with some advanced devices, it allows movement of the wrist and specific grip patterns(25).

Figure 5: A Typical Below The Elbow Prosthesis

Transhumeral(above the elbow): At this level, very few transplants of the hand have taken place, and they are not favorable for hand transplantation. This is because the distance for nerve regeneration and the number of muscles that need to be reinnervated are of major concern at transhumeral level(26). Since not only the environment inside the body is not active during the months of nerve regeneration, but also all the muscles of flexion and extension of the wrist are not active, the course of recovery is also prolonged and contributes to additional recovery to the motor activity.. Due to these factors, a conventional myoelectric upper arm, which is controlled by surface electrodes that are sourced by completely separated innervated muscle groups. Furthermore, since the prosthesis usually compromises of an elbow joint , a wrist joint and a terminal device(hand or a hook), the user has to alternate the control between these parts, therefore, traditional control of transhumeral prosthesis is slow and unintuitive. These factors make a hand prosthesis an indication in transhumeral amputation as well.

Figure 6: Transhumeral Hand Prosthesis

Shoulder: This type of amputation is a typical marker of Targeted Muscle Reinnervation(TMR) but prosthetic reconstruction with a myoelectric shoulder joint can only be performed in a laboratory at present.(19). At this level of amputation, limb transplantation is not considered feasible due to the increased distance required for nerve regeneration and the need to reconstruct additional joints, thereby making a hand prosthesis the absolute indication.

Figure 7: An Example of Myoelectric Prosthesis

9. Pros and Cons of Hand Transplantation and Modern Hand Prosthesis

Hand allotransplantation, a type of Vascularized Composite Allotransplantation (VCA), provides considerable benefits in restoring form and function. However, it also poses significant immunological risks and long-term health challenges. Among the most noticeable is the high incidence of acute rejection that follows transplantation of tissues or organs in about 85 percent of the recipients, especially the skin, because of high immunogenicity of the transplanted tissues or organs(27). Other challenges are described later while talking about the cons of hand transplantation.

9.1 Pros and Cons of Hand Transplantation.

The primary aim of hand transplantation is to achieve useful long-term function and graft survival, offering different distinct advantages over traditional prostheses. The biggest advantages of hand transplantation are mentioned below.

Restoration of sensory and motor function is the biggest advantage of hand transplantation, as, unlike a prosthesis, a complete and successful transplant can restore fine motor movements, which allows the patients to carry out tasks of daily life like tightening buttons and driving(28). Moreover, it also restores many other modalities, including touch, proprioception, vibration, temperature, and pain.

One of another advantage of hand transplantation is that it adds to the psychosocial and aesthetic benefits as the procedure adds to the restoration of the patient's body image and “individuality” through an aesthetically pleasing result(29). Most patients report a higher satisfaction rate with psychosocial outcomes.

Successful transplants result in increased independence, which allows patients to regain autonomy, often enabling them to return to activities of a high skill level that would be impossible with a prosthesis, thereby adding to the advantages of hand transplantation (30).

Moreover, the usage of tacrolimus in the immunosuppressive regimen has shown to have nerve regenerative properties(31), which helps to increase axonal diameter and myelination, further improving. Due to the use of tacrolimus, faster functional recovery and a reduced time period of denervation should be highlighted as an advantage of hand transplantation(32).

Another added advocate for hand transplantation is the fact that visible monitoring is easy, whereas compared to other organs (like a lung), a hand transplant allows direct inspection of the hand, and signs of rejection can be noted if present, making it easier to identify and treat as early as possible(33).

Figure 8: Successful Hand Transplant.

With such added advantages, hand allotransplantation also comes with quite a few drawbacks that are worth mentioning; the most important drawbacks of hand allotransplantation grow from the medical requirements to prevent the body from rejecting the donor tissue(30).

The biggest drawback of hand transplantation involves the use of lifetime immunosuppressive medications(19). There can be many side effects to immunosuppressive medications. The most common and well-known side effects include metabolic dysfunction (diabetes, hypertension), organ failure, more commonly kidney failure due to improper excretion of medication, neurotoxicity, and an increased chance of opportunistic infections and cancers, which can include skin, mouth, and esophagus cancer(34).

In hand transplantation, there is a higher rate of rejection even with immunosuppressive medications; it is stated that 85% of recipients within the first year experience acute rejection, and 60% are susceptible to recurrent rejection(35). As rejection stands, there are 3 types of rejection: hyperacute rejection, acute rejection and chronic rejection. The most challenging rejection to be solved among the three types that are in transplants is the chronic rejection. Hyperacute rejection happens within the space of minutes to hours, owing to the presence of preformed antibodies and is mostly avoidable through the appropriate donor-recipient matching plus cross-matching methods(36). Acute rejection occurs within days to months and usually resolved by hastening immunosuppressive therapy (37). However, chronic rejection is cardiac, accumulative, over months to years, and is progressive and determined by vascular damage, fibrosis and permanent graft failure. Moreover, the literature indicates that after developing, chronic rejection is irreversible and it may only be slowed down, so prevention is the primary tool(37)(38). So, chronic rejection is regarded as hardest to treat and the least reversible type of transplant rejection.

Besides these physiological issues, other significant variables like psychology and adherence of the patient are important in the long term success since inability to adhere to the complex immunosuppressive regimens can directly result into graft rejection and loss(39) .

I believe another drawback arises from the ethical background, because hand transplantation is intended to improve the quality of life, rather than saving life. There is indeed a continued ethical discussion on hand transplantation, whether the benefits outweigh the risks of lifelong medications to suppress the immune response.

9.2 Pros and Cons of a Hand Prosthesis.

The evolution of upper-limb prostheses presents strong advantages to people have lost their limbs, yet, these implants also have serious technical, physical, and financial issues. According to the sources, the main strengths and weaknesses are as follows.

One of the advantages of hand prosthesis is same as hand transplantation which is the functional restoration of hand. Modern hand prosthesis aims to restore normal daily functions. According to group of scientists from Yale University(40) mentioned advance human-like hand with polyarticulated fingers can potentially improve dexterity , whereas intelligent control can provide reflex-like actions , such as autonomous slip prevention.

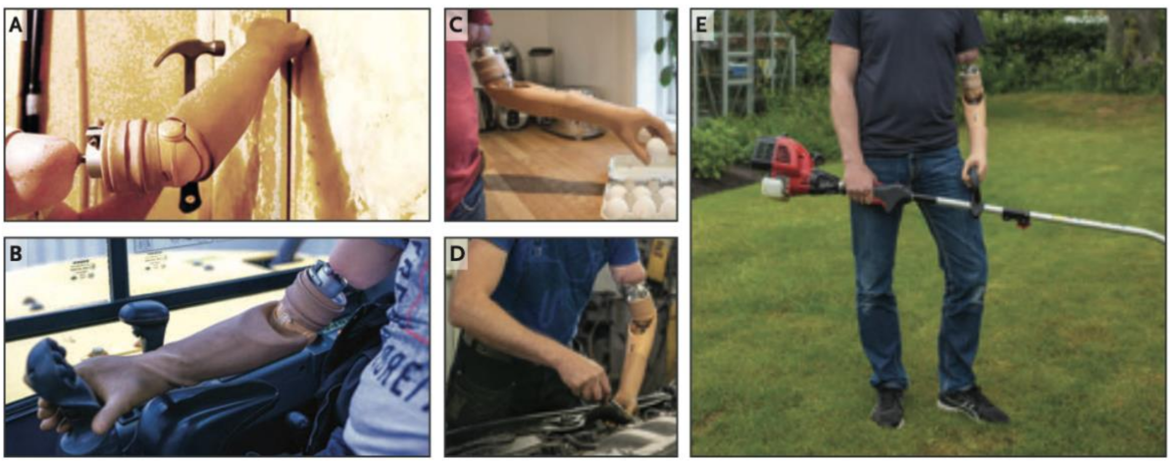
Moreover, the most significant advantage of hand prosthesis is avoidance of immunosuppressive medications which must be taken life-long. Hence this avoids the risks associated with immunosuppressive medications(28).

When a hand prosthesis is fitted after the injury occurs the process involves a short hospital stay and rehabilitation period compared to hand allotransplantation in which rehab is longer , making it a huge advantage for hand prothesis to be preferred over hand allotransplantation.

Motor function in modern myoelectric prostheses is comparable to functional outcomes observed in hand transplantation, as both approaches enable performance of essential activities of daily living, with some studies reporting no significant difference in general motor outcomes at all(41).

Some of the few drawbacks of hand prosthesis include problems with detailed task performance patients may have problems with precise motor actions or detail tasks, e.g. thread through the needle, since they do not receive fine tactile feedback(28). This is because hand prosthesis is programed to move in certain variations without any control, where as a hand moves in certain direction with full control by an individual, hence precise motor skills are important which are lacked in hand prosthesis. In Figure 9 some of the prosthesis used in daily life work which needs precision can be seen.

Figure 9: Arm prosthesis used in daily life



With hand prosthesis there are aesthetic and psychosocial limitations , while transplant patients can restore a patients “individuality” and body image, unfortunately prosthesis may not provide same level of psychosocial satisfaction(42). This can be as a result of the fact that the person can feel that the hand prosthesis is not part of his body.

The deficiency of sensitivity is also a significant drawback. In contrast to a transplant, which has the power to recover touch, temperature and proprioception, a prosthesis does not provide any form of sensory feedback and therefore it is hard to get bilateral amputees to perform tasks without visual feedback(41).

10. Future Perspectives

In the near future , hand transplantations will probably continue to be of a fairly limited surgical procedure. The technical difficulty of the surgery is not trivial but it can still be overcome with time, with the help of technical expertise of the experienced hand and microsurgical staff because all of them have previous experience in the field of replantation an example of the team is shown below in Figure10 . Similarly immune suppression medications have been evolved with great success in reducing rejection irrespective of difficulties associated with transplantation of skin. As discussed earlier the smooth function of the hand has had an impact on the quality of life, however current data on hand transplant suggest, unlike other organs transplant hand transplant does not increase the lifespan on an individual, which may raise even more ethical concerns in near future.

Figure 10: Hand Transplantation Team in Operating Room

This choice now is even more complicated by the production of the prosthetic and rehabilitation technologies that have delicately advanced throughout the last 20 years. Surgical innovations including targeted muscle reinnervation and osseointegration will still improve the work of prosthetic devices, and the threat to patients is much less relative to the practice of transplanting hands as, in addition, standardized rehabilitation regimes will allow people to learn to set specific goals and monitor their progress throughout their lives(43). Nevertheless, patients cannot use the prosthetic device without direct visualization until this is resolved by sensory input with the assistance of these devices. Nonetheless, this is also getting narrower, and new studies show promising applications of sensory feedback into the prosthetics(44). In the future, it is anticipated that the future research projects undertaken will remain parallel in many aspects. Further follow-up of the current set of transplant recipients will offer information on better medical treaties in the long term. Further initiatives in cortical mapping and rearrangement after the loss of limbs, transplantation and uptake of prosthetics will also come into play in determining whether a perfect incorporation of these technologies is possible or not. Hopefully, in the future, with the current effort in limb regeneration, the therapies might have no further need, but in the meantime, a lot could be learnt about the role of maximizing return of function in patients who have suffered amputations of limbs(43).

The future of hand prosthesis is moving at quite a rapid pace towards creating solutions that is a mix of advanced surgical techniques with experienced technological interfaces to get the better of these issues that include comfort , weight and function(45). In mid 2010s the first successful proof of concept for modern bionic arms was found, which involved bi-directional between device and nervous system.

Figure 11: Bionic Arm prostheses

The main aim of bionic technology is to mimic the almost natural behaviour of a healthy limb by using sophisticated biological-technological combination. This is through three major forms of tissue interfacing. First, targeted muscle reinnervation (TMR) is the redirecting of the remaining peripheral nerves of the amputated limb to the surrounding muscle, like the chest, which serve as biological amplifiers of neural impulses that can be recorded by surface electrodes to operate the prosthesis. Second, direct muscle interfacing involves the use of implanted recording devices in the residual muscles to record electrical activity produced upon muscle contraction and wirelessly transmitted to cause movement in prosthetics. Lastly, the most advanced form is direct nerve interfacing, where electrodes are implanted into or around peripheral nerves, allowing not only motor intent to be detected, but also bidirectional communication, which allows sensory feedback, such as touch perception, to be sent back to the user, increasing the control and embodiment of the prosthetic(46).Researches hold the belief that the next generation of bionic limbs will have the capability to utilize osseointegration for direct mechanical bone attachment alongside the sensors , which will be able to provide more reliable and wireless control(47).

As more innovation is being integrated into prosthetic limb the cost of the limbs are becoming expensive. The cost of prostheses varies depending on the complexity of the technology Basic body-powered prostheses typically cost between $3,000 and $10,000, whereas modern myoelectric prostheses range from $9,000 to over $40,000(48), however advanced bionic prostheses which are equipped with multi-grip systems and neural interfaces may exceed €50,000 and are associated with higher long term costs as compared to conventional devices(49) These are annual prices not just the device price, they include maintenance, replacement and follow-up care, hence making it a long term economic burden.

At the end this field is now focusing towards a patient-centered-decision making process to make sure that the cost of prosthesis are in such a way accustomed to special functional and social needs of the users, hence reducing the abandonment rate currently seen in clinical practice(50).

11. Results

11.1 Evaluation of the Performances of Commercially Available Hand Prosthesis

A study conducted in 2024(37) measured performance of different hand prosthesis commercially available .

11.2 Methods

Anthropomorphism Hand Assessment Protocol (AHAP) was the metric of evaluation that was used (52). This is a validated procedure that was invented by other people as a benchtop test where household objects are held and grasped. It is applied to determine the mechanical grasping strength of dexterous prosthetic hand with numerous gripping positions and is intended to be conducted without the involvement of a prosthesis. In other words, the hand by itself is under scrutiny and not the potential confounding factors which include the type of control system used, the fit of the prosthetic socket or the level of skill demonstrated by the user in operating their device amongst several others. The AHAP is administered with 26 discrete tasks with the use of 25 household items and comprising 10 grip patterns: hook grip, spherical grip, tripod pinch, extension grip, cylindrical grip, diagonal volar grip, lateral pinch, pulp pinch, index pointing/pressing and platform.

The reliability of the AHAP is also high with test retest reliability intraclass correlation coefficient (ICC) of 0.839, inter-rater reliability ICC of 0.969, and internal consistency Cronbachs alpha of 0.846 (52). To analyze it, they identified three open-source 3D-printed prosthetic hands, including HACKberry Hand, HANDi Hand, and BEAR PAW seen in Figure 12, and three commonly prescribed, Clinical Prescribable and Commercially Available prosthetic hands, such as Ossur i-Limb Quantum, RSL Steeper BeBionic Hand V3 and Psyonic Ability Hand(51), these can be seen in Figure 13.

Figure 12: 3D- Printed Prostheses

Fig. 5 HACKberry hand

Fig. 6 HANDi hand

Fig. 7 BEAR PAW

Figure 13: Clinical Prescribable and Commercially Available

Fig. 2 Össur i-Limb quantum

Fig. 3 RSL steeper BeBionic V3

Fig. 4 Psyonic ability hand

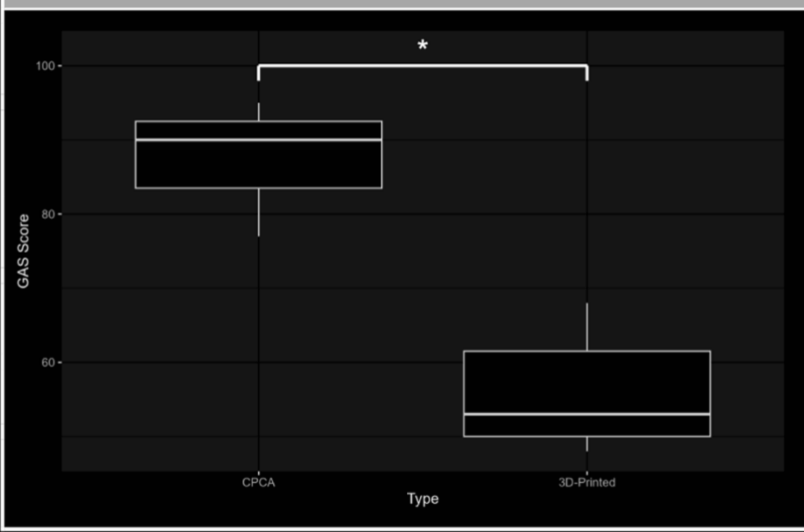
In accordance with AHAP protocol(52) , the scoring of the performance of the prosthesis was conducted at the grasping and maintaining stages of each of the objects by the lead investigator. In this respect, the score of 1 was obtained in case the object was held using the given grip during the duration provided. When the prosthesis was able to hold the object during the required time but failed to meet the requirements of the specific grip as detailed by the AHAP, a score of 0.5 was awarded. . In the end, score 0 was obtained in case the prosthesis could not hold the object at all. Then, in case there was no movement of the object in the hand at the maintaining stage, a mark of 1 was given. In the case of movement of the object, which did not result in a drop, a score of 0.5 was obtained and 0 in the case where it could not hold the object. The lead investigator in that study can also assign a score of 0 at his discretion and without making an attempt at the grip when it was considered that an attempt would result in functional loss to the hand.

11.3 Results for Performance of Commercially Available Hand Prostheses

Overall Performance with Clinical Prescribable and Commercially Available hands which included Ossur i-Limb Quantum, RSL Steeper BeBionic Hand V3 and Psyonic Ability Hand were far much better than 3D-printed hands which included HACKberry Hand, HANDi Hand, and BEAR PAW. Clinical Prescribable and Commercially Available devices had a median grasping ability score of 90% with a 3D-printed hand having a median of 53%. This is because the initial null hypothesis was group of prosthesis showed identical underlying distributions. The null hypothesis was rejected the P-value was 0.0083 which was less than 0.0167 which was the threshold P-value These were calculated using Mann-Whitney U- test results shown in Figure 14 below.

Figure 14:Overall Grasping Ability Score Mann-Whitney U-test results:

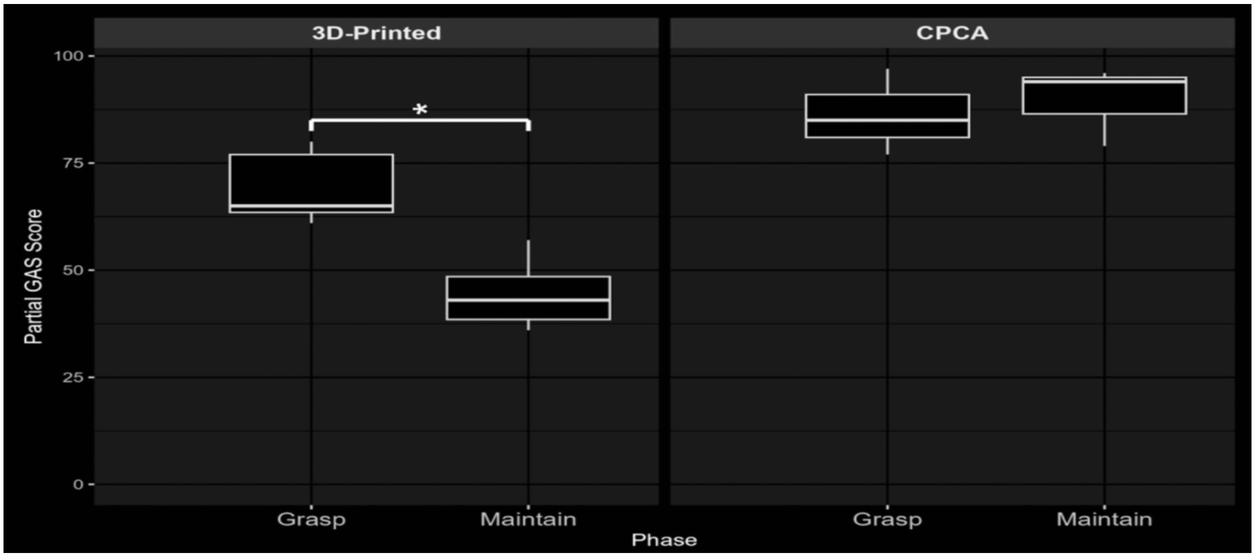
GAS Score Comparison Between CPCA and 3D-Printed Prostheses



Range	Clinical: 18	
	3D-printed: 20	
Median	Clinical: 90	
	3D-printed: 53	
Test Statistic	21	
P-Value	0.0083	

The results of the phase-specific performance in which the AHAP assesses hands in two stages: grasping (first pick-up of the object) and holding (holding the object in rotating the hand 180 degrees), are as follows in Figure 15.

Figure 15:Comparing grasping vs. maintaining scores



Stability in Clinical Prescribable and Commercially Available Hands: There was no statistically significant difference in phases in these devices (p=0.50), i.e. they were not better at noticing an object and during movement, there was a high probability that they would retain it(51).

Large Decrease in 3D-Printed Hands: These hands faired much lower in the maintaining stage (p=0.0011). When the HACKberry Hand was used as an example, the 64% grasping score seemed to have decreased to 36% maintaining score. It implies that although 3D-printed hands can sometimes be able to begin a grip, they are not as mechanically stable or possess as much friction to hold the objects in place during manipulation(51).

Lastly some challenges were noticed with specific grip patterns. It was found that some of the grips were significantly harder on the prostheses compared to others. The grips tested are illustrated in Figure 16 below.

Figure 16: Different Types of Grips Tested

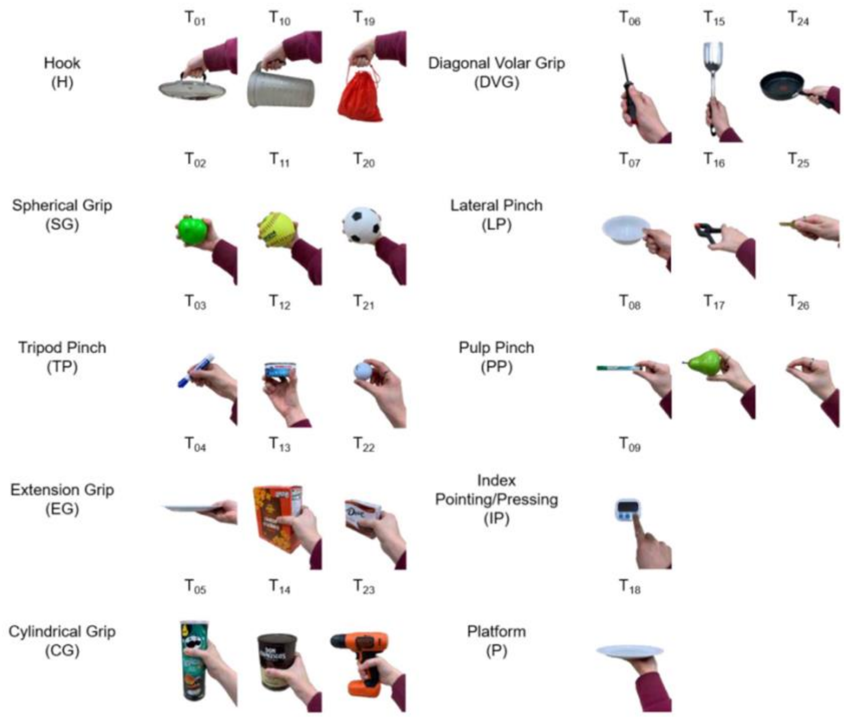
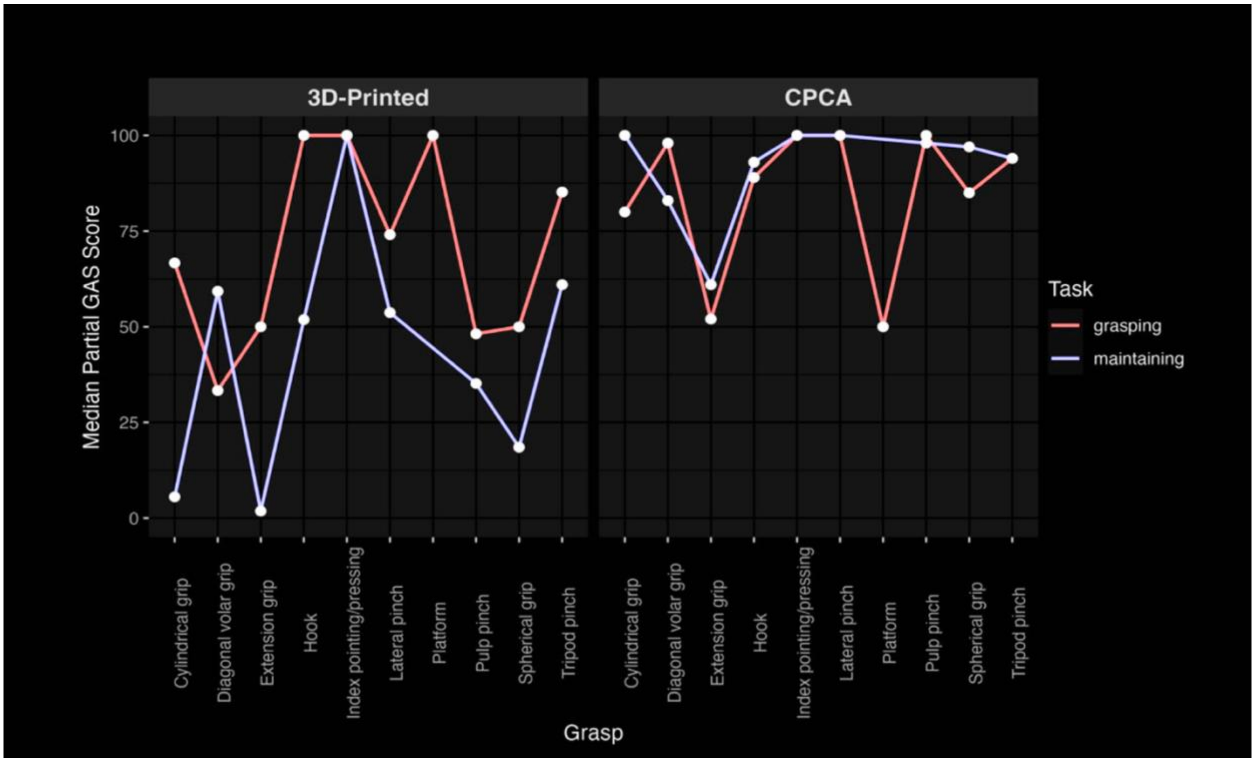


Fig. 1 AHAP tasks and grips

The hands using 3D-Printed prosthesis had the worst time with Diagonal Volar grip during the grasping stage. In maintaining stage, they especially had the tendency to drop objects with the use of Cylindrical, Extension and Spherical grips(51).

Clinical Prescribable and Commercially Available hands were very good except that Clinical Prescribable and Commercially Available hands were slightly poor with Extension and Platform grips at the stage of initial grasping(51). Rest of the results are summarized in Figure 17.

Figure 17: Grip-wise comparison using Friedman's test



The general findings of the paper are that it is possible to draw the conclusion of a significant difference in performance of clinically prescribable and commercially available prosthetic hands and 3D-printed ones. Although filament-based hands have a considerable higher cost benefit 3D-printed hands, they have a lower technology readiness level to use in practice.

11.4 Functional and Psychosocial Outcomes of Hand Transplantation Compared with Prosthetic Fitting

A multicenter cohort study published in 2016 (41) measured the functional and psychosocial outcomes of hand transplantation compared with prosthetic devices. These were carried out in below-elbow amputees.

11.5 Methods

The method of the study was to assess hand function in amputees with either a transplant or a prosthesis, and they were tested with ARAT, SHAP, and DASH. Also, quality-of-life was compared with the Short-Form 36(SF-36).

Twelve patients who underwent either hand transplantation (n=5, Group1) or prosthetic fitting (n=7, Group2), after below-elbow amputation, and had completed rehabilitation and gave written consent to take part in this study.

Exclusion criteria in this study were patients with visual impairment and those who were not available for functional and psychosocial assessments.

11.6 Functional Outcome Measures and Quality of Life Assessments

ARAT is an observational test used to assess the upper-limb motor function. It consists of 4 subscales: Grasp (18 points), Grip(12 points), Pinch (18 points), and Gross movements(9 points), making up the total score of 57 points(53). SHAP is a clinically validated test for assessing hand function, which was originally developed to assess the effectiveness of upper limb prostheses. It is made up of 8 abstract objects, which include 14 activities of daily living (ADL), in which each task was timed by participants themselves. Normal hand function resulted in 100 points in SHAP. Lastly, bimanual tasks in daily life were rated using DASH, which is a questionnaire in which a score of 100 correlates with the worst and 0 indicates the best hand function(41).

Patient's quality of life and overall life satisfaction were evaluated via SF-36. SF36 contains an 8-scale profile of functional health and well-being scores along with psychometrically based physical and mental health summary measures and a preference-based health-utility index. Overall, SF-36 provides a general quality of life assessment by measuring four scales, each of them for physical and mental health(41).

11.7 Statistical analysis

The SHAP and SF-36 scores were compared between two separate groups. Since the data were not paired and did not follow a normal distribution, a Mann–Whitney U test was used. A p-value of less than 0.05 was considered statistically significant. The analysis assumed that both groups had similar average scores unless proven otherwise.

11.8 Results

Firstly, we will look at the functional outcomes in the transplanted patients and the hand prosthesis patient. The results are summarized in Table3 below.

Table 3 : Functional Outcomes

	Hand	Patient	Side	DASH	ARAT	ARAT healthy	ARAT percent of healthy hand	SHAP	SHAP healthy	SHAP percent of healthy hand
Group 1 Transplant	1	1	right	27.00	50	bilateral	bilateral	84	bilateral	bilateral
	2		left	27.00	42	bilateral	bilateral	75	bilateral	bilateral
	3	2	right	55.00	31	bilateral	bilateral	72	bilateral	bilateral
	4		left	55.00	33	bilateral	bilateral	72	bilateral	bilateral
	5	3	right	8.00	44	57	77.19%	88	99	88.89%
	6	4	right	8.33	42	57	73.68%	80	101	79.21%
	7	5	right	14.17	35	57	61.4%	54	97	55.67%
		Mean/SD		**22.5 ± 19.73**	**40.86 ± 8.07**	**57.00 ± 0**	**70.76 ± 8.29**	**75.00 ± 11.06**	**99.00 ± 2.00**	**74.59 ± 17.09**
Group 2 Prostheses	1	1	left	7.50	42	54	77.78%	83	99	83.84%
	2	2	left	10.00	35	57	61.40%	75	97	77.32%
	3	3	right	20.83	42	57	73.68%	78	96	81.25%
	4	4	right	17.50	38	57	66.67%	54	97	55.67%
	5	5	left	9.17	36	57	63.16%	70	99	70.71%
	6	6	right	1.67	44	57	77.19%	85	98	86.73%
	7	7	right	9.17	36	57	63.16%	83	98	84.69%
		Mean/SD		**9.83 ± 6.95**	**39.00 ± 3.61**	**56.57 ± 1.13**	**69.01 ± 7.04**	**75.43 ± 10.81**	**97.71 ± 1.11**	**77.17 ± 10.90**

It can be noted that transplanted patients achieved a mean ARAT of 40.86± 8.07. The average SHAP score of this group of transplanted patients was 75.00 ± 11.06, with the DASH group projected as an average of 22.50 ± 19.73. Meanwhile, it can be noted that the mean ARAT of prosthetic patients was 39.00 ± 3.61; moreover, the average SHAP score was 75.43 ± 10.81, and the average DASH score was 10.83 ± 6.40. Statistically, there was no significant difference in the ARAT (p=0.87), SHAP (p=0.98), and DASH (p=0.40)(41). Overall, there was no significant difference in the functional outcome between the function of hand transplantation and hand prosthesis.

The transplant patients showed significantly higher scores in the psychosocial outcomes summarized in Table 4.

Table 4: Psychosocial outcomes

		T-values							
	Patient	Physical functioning	Role physical	Bodily pain	General health	Vitality	Social functioning	Role-emotional	Mental health
Group 1 Transplant	1	53[A]	58[A]	57[A]	51[A]	**64**[AA]	57[A]	54[A]	**61**[AA]
	2	48[A]	56[A]	**37**[BA]	42[A]	57[A]	57[A]	54[A]	59[A]
	3	56[A]	56[A]	55[A]	50[A]	**60**[AA]	**26**[BA]	54[A]	**60**[AA]
	4	54[A]	53[A]	48[A]	50[A]	**65**[AA]	54[A]	53[A]	**64**[AA]
	5	44[A]	53[A]	42[A]	**39**[BA]	54[A]	54[A]	53[A]	59[A]
	Mean/ SD	**51.00 ± 4.90**	**55.20 ± 2.17**	**47.80 ± 8.47**	**46.40 ± 5.50**	**60.00 ± 4.64**	**49.60 ± 13.28**	**53.60 ± 0.55**	**60.60 ± 2.07**
Group 2 Prostheses	1	49[A]	52[A]	50[A]	41[A]	46[A]	54[A]	53[A]	54[A]
	2	**39**[BA]	44[A]	41[A]	**35**[BA]	48[A]	55[A]	53[A]	49[A]
	3	**34**[BA]	**10**[BA]	**28**[BA]	**36**[BA]	46[A]	**39**[BA]	53[A]	54[A]
	4	44[A]	**24**[BA]	55[A]	58[A]	51[A]	54[A]	53[A]	57[A]
	5	49[A]	**10**[BA]	55[A]	53[A]	51[A]	54[A]	**36**[BA]	47[A]
	6	54[A]	53[A]	48[A]	**39**[BA]	51[A]	54[A]	53[A]	52[A]
	7	**39**[BA]	**24**[BA]	55[A]	55[A]	57[A]	54[A]	53[A]	55[A]
	Mean/ SD	**44.00 ± 7.07**	**31.00 ± 18.59**	**47.43 ± 9.98**	**45.29 ± 9.71**	**50.00 ± 3.83**	**52.00 ± 5.74**	**50.57 ± 6.43**	**52.57 ± 3.51**
Mann-Whitney U test		**0.144**	**0.006**	**0.975**	**0.908**	**0.008**	**0.487**	**0.035**	**0.003**

[BA] below average.
[A] average.
[AA] above average.

People who received hand transplants scored higher in areas such as physical roles, energy levels, emotional roles, and mental health. In other areas like physical functioning, pain, general health, and social life, there were no clear differences between transplant and prosthetic users. Most transplant patients reported quality-of-life scores that were like those of healthy men of the same age. Two of them even felt more energetic and mentally well than average. However, one transplant patient reported some difficulty with social activities, and another felt their general health was below average(41). Overall, the transplant group reported a good quality of life and were generally happy with both how their hands worked and how they felt psychologically.

People using prosthetic hands were also mostly satisfied with their devices. Some reported challenges with physical and emotional roles, as well as general health. Except for one individual, most prosthetic users had quality-of-life scores like those of men of the same age(41)

11.9 Limitations

Hand transplantation has been performed in only a small number of people, since upper limb amputees themselves are a relatively rare group. Because of this, comparisons between transplant and prosthetic patients depend largely on who is available to take part in studies. This makes it difficult to ensure that the groups are truly comparable. In this study, patients with very different levels of disability were compared, which may have affected the results. This is especially important when looking at psychological and social outcomes, as losing both hands is clearly more life-changing than losing one. Future research would benefit from comparing patients with similar types of amputations, such as bilateral versus unilateral cases, and matching patients based on the level of amputation. In addition, as prosthetic technology continues to improve and begins to restore sensation, it may be important to re-evaluate whether hand transplantation still offers a clear advantage in terms of sensory and motor function.

12. Discussion

Hand transplantation represents a complex perspective of actually restoring the functionality of hands alongside sensation and self-esteem and consequently improves the quality of life in amputated individuals in the upper limbs . However, a lot of years since first successful transplantation of the hand in human and having had more than 100 transplanted limbs throughout the world, composite tissue transplantation remains a debatable issue in the hand surgery community (30). Even though loss of limbs is not a life-threatening disorder, loss of one or both hands causes severe dysfunctions along with enormous psychosocial burden (54). The positive outcomes of the motor and sensory restoration could outweigh the adverse effects of the immunosuppression in bilateral loss of limbs hence would be better than the outcomes of the amputation of the hand below the elbow joint (41). Since unilateral amputees can partially cover most of the functional impairment with their intact healthy hand and a prosthesis, the hand transplantation indication should be narrowed to bilateral below-elbow limb losses(41). The best potential patient would be a patient that is already under immunosuppression because of a life threatening condition and has lost both his hands(19). All the merits of hand transplantation would be used in this patient without extra hazards . Even though other patients have claimed that they had activities such as the heavy lifting which are easier with the prosthesis, hand transplantation overall results in better functioning and psychosocial outcomes than any existing prosthetic device in below-elbow amputees (41). Overall, the commercially available prosthesis the studied showed that of clinically prescribable and commercially available prosthesis were better in functionality which was tested using AHAP as compared to that of 3D-Printed ones.

13. Conclusions

1. The most typical indication of hand transplantation is bilateral below-elbow amputation, in which hand transplantation has the best chance of producing functional outcome.

2. Hand allotransplantation offers considerable benefits such as restoring motor and sensory functions and other valuable psychosocial and aesthetic ones, enhancing body image and a sense of individuality, but its biggest weakness is that it requires life-long immunosuppression, which has severe long-term risks. On the other hand, prosthetic devices can be used to restore hand functionality without immunosuppressive treatment but are frequently costly and can be restricted in their ability to make fine and precise movements necessary to complete complex tasks.

3. In the future, bionic prosthetic arms will be the future of limb reconstruction, as increasingly neural interfacing, sensory feedback, and artificial intelligence are allowing more natural and intuitive control. These advances imply that bionic technology will one day possibly fill the gap between prosthetic replacement and biological restoration, with better functional results and without the medical risk of transplantation.

4. Conclusively, there is no substantial difference in the performance of Clinical Prescribable and Commercially Available and Modern Prosthetic use has been found when measured using standardized test called Anthropomorphism Hand Assessment Protocol. This implies that both prostheses can be used to rehabilitate a similar degree of functional performance in activities of daily living.

5. Lastly, the hand transplantation and the prosthetic fitting were compared and it was found that there is no significant difference in the functional outcomes of the two approaches due to non-parametric data distribution using standardized tests and assessing them using the Mann-Whitney U test. This shows that either hand transplantation or prosthetic devices can be used to attain similar degrees of functional performance in everyday activities. Nevertheless, the major difference was noted on psychosocial outcomes, as transplant recipients scored much higher on such domains as physical role functioning, energy levels, emotional well-being, and overall mental health. These results shows that

although functional restoration might be comparable, hand transplantation has some other advantages in terms of psychological integration, quality of life, and patient satisfaction, which makes it important to consider both functional and psychosocial issues when choosing the best treatment option.

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