

The health technology assessment of the compulsory accident insurance scheme of hand transplantation in Switzerland

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Abstract

Recently the decision-making committee of the compulsory Swiss accident insurance scheme needed to make a basic decision as to whether to fund hand transplantation under that scheme or not. A Health Technology Assessment was commissioned to inform decision-making and gain experience with applicability of the method. The following were main findings from various domains. Compared with prosthesis fitting, the outcome of hand transplantation is satisfactory for function and sensibility. Complications due to immunosuppression are frequent, sometimes severe and potentially life-shortening. The direct medical costs over the entire life span calculated for a 35-year-old unilaterally amputated base case patient were CHF 528,600 (EUR 438,500) higher than for a prosthesis. There are challenging ethical, legal and organizational issues. The committee decided not to reimburse hand transplantation for ethical reasons. The Health Technology Assessment has been shown to be a useful tool for decision-making in the context of Swiss accident insurance.

Level of evidence: IV

Keywords

Hand transplantation, reimbursement, costs, evidence-based health care, health technology assessment, immunosuppression

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Introduction

The adoption of hand transplantation remains restricted more than 15 years after the first successful such procedure in 1998 in Lyon (Dubernard et al., 2000). Only about 50 hand transplantations have been performed worldwide (status: April 2012) and documented in the International Registry on Hand and Composite Tissue Transplantation (IRHCTT, 2012). Controversial medical and ethical issues revolve mostly around the following two topics: (1) improvement in upper limb function is limited and (2) potentially harmful immunosuppression is needed for the rest of a patient's life after treatment of a non-life threatening problem. Another controversial issue is the high additional cost compared with the standard prosthetic treatment.

In Switzerland, no hand transplantation has been performed to date. In 2011, a patient with a forearm amputation applied for the reimbursement of the cost of a hand transplantation under the compulsory accident insurance scheme. His hand surgeon was ready

to perform the first such procedure at a Swiss university hospital. The accident insurance company found it difficult at the time to make the first such funding decision. Therefore it turned to the committee for compulsory accident insurance called 'Medical Tariff

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Committee for the Swiss National Accident Insurance' (MTK UVG) to make a fundamental decision.

To understand the institutional context of that decision one needs to know that there are two independent social insurance systems for health care in Switzerland. First, there is compulsory health insurance that every inhabitant of the country must have. Second, there is social accident insurance that is compulsory for all people in salaried employment. For others, such as the elderly, children, students or the self-employed, health insurance also covers the costs of medical treatment in the case of accidents. Accident insurance in general, however, has more generous benefits than health insurance. For instance, it also covers loss of working hours. The two parallel systems have evolved historically. The compulsory accident insurance scheme is operated by one large national insurance company with a partial monopoly for the employees in the manufacturing sector and several private insurance companies that compete for the employees in the service sector.

The committee (MTK UVG) is concerned with the regulation of all fundamental questions for the whole area of compulsory accident insurance. It consists of ten members representing the different insurer categories. Two members of the committee are medical doctors. Traditionally the committee is concerned with tariff and legal issues. The committee was aware that they were going to make a fundamental decision on a specific medical technology for the first time. In order to have a sound basis for such a decision, a university research institute was commissioned to conduct a Health Technology Assessment (HTA).

The method of a HTA can be described as an aid for decision-makers at the health system level that helps make coverage decisions. These decisions have to be made with a degree of uncertainty and they need to integrate aspects of risks, benefits, costs and values of patients. HTA uses techniques of evidence-based medicine and decision-analytic modelling typically applied in health economics. An HTA report is a multidisciplinary study that analyses medical, social, ethical and economic implications of development, diffusion and use of health technologies (INAHTA, 2014).

Despite its broad interdisciplinary definition, most HTAs only deal with medical (effectiveness and safety) and sometimes economic (cost-effectiveness and budget impact) aspects. In the case of hand transplantation, however, it was decided to cover the full range of domains and to include the potentially controversial ethical, legal and organizational aspects as well. An HTA itself does not conclude or make recommendations as to whether or not to reimburse a particular medical intervention such as hand transplantation.

That decision is up to the decision-maker (here the committee MTK UVG), which can use its judgement of the facts presented and has the freedom to consider additional factors not covered in the HTA report.

The reported HTA had two aims: first to support the committee in making a fundamental decision whether to reimburse hand transplantation in Swiss accident insurance; and second to be a pilot case for the methodology and the process of a HTA. In this article, we report on the methods and the findings of this HTA and also on the final decision taken by the committee.

Methods

A HTA methodology was applied and a report for decision-making was generated by a research institute specializing in HTA methodology. An expert group was established that consulted the project team. It consisted of two senior hand surgeons, a medical doctor specializing in health insurance claims and a bio-ethicist. The structure of the HTA report was inspired by the EUnetHTA core model (EUnetHTA, 2014).

The following scientific questions were posed in the HTA report:

1. *Medical questions.* How effective and safe is the hand transplantation in comparison with prosthesis fitting?
2. *Economic questions.* What is the cost of hand transplantation in comparison with prosthesis fitting from the perspective of social accident insurance in Switzerland? What is the cost-effectiveness of the hand transplantation in comparison with prosthesis fitting? How many cases are to be expected in the future in Switzerland (budget impact)?
3. *Ethical/legal question.* What are the ethical and legal implications that should be considered?
4. *Organizational question.* What are the organizational implications for the Swiss healthcare system that should be considered?

A variety of data sources were used. First, a literature search in electronic databases (Medline; Cochrane Library; HTA-Database; DARE-Database) was performed in October 2011, based on current guidelines (Centre for Reviews and Dissemination, 2009). The search terms (MeSH terms) were 'transplantation', 'hand', 'treatment outcome', 'quality of life', 'graft rejection', 'musculoskeletal physiological phenomena', 'costs and cost analysis'. Inclusion criteria mainly focused on all study designs, adult patients (18–65years), single or double hand transplantation

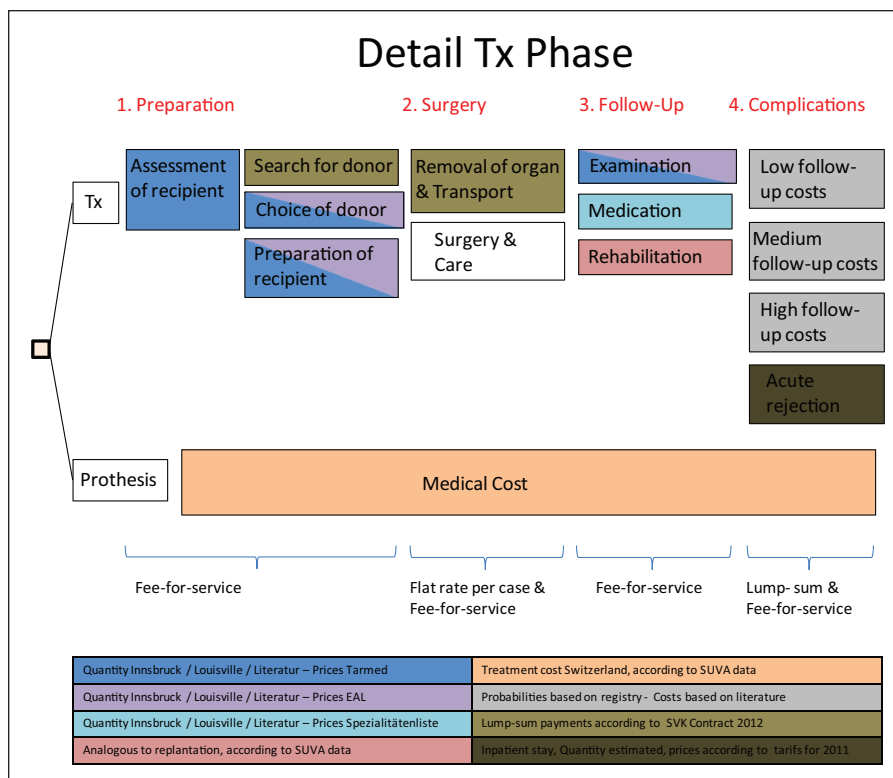


Figure 1. Cost model.

Tarmed: Swiss system of tariffs for procedures codes; EAL: Swiss system of tariffs for laboratory analysis; SVK: Association of Swiss health insurers

and different outcomes such as costs, functionality or complications. A focused hand search of specific journals in the field of hand transplantation was conducted, e.g. the *Journal of Hand Surgery (American Volume)*, the *Journal of Hand Surgery (European Volume)* and *Transplantation*. A scoping literature search for hand prosthesis fitting was performed. In addition, several experts in different fields of hand transplantation were interviewed (hand surgeons, transplantation specialists, ethicists, legal specialists). Furthermore, on 10 January 2012 the research team made a site visit to the hand transplantation programme in Innsbruck, Austria. Valuable and in-depth information on the procedure (including the treatment protocol) was obtained. Finally, Swiss cost data was derived from various sources, such as tariffs, as well as cost data from the national Swiss accident insurer.

An economic cost model was developed. A model patient was used for the calculation. The following assumptions were made: The model patient at the time of unilateral forearm amputation was 30 years old. During the first 5 years the patient was treated conventionally with a prosthesis. From the age of 35 onwards, a scenario with hand transplantation and a scenario with persistent prosthetic treatment were modelled. At the time of transplantation, the patient

has a life expectancy of a further 46.1 years (average life expectancy for men in Switzerland in 2010 (Bundesamt für Statistik, 2010). The treatment with transplantation requires life-long immunosuppression resulting in an associated increased risk of several diseases (e.g. arterial hypertension, [transient] renal impairment, recurrent infections and malignancy). Therefore, we assumed a shortened life span of 3 years in comparison to the treatment with a prosthesis.

The costs were calculated in different blocks (Figure 1). Various data sources were used. A treatment path was generated with the help of the Innsbruck protocol, literature and expert input. To obtain costs, the quantities in the treatment path (number of days in hospital, doctor visits, medication etc.) were multiplied by Swiss prices or tariffs, respectively. Where there was a lack of information on Swiss costs because no hand transplantation had been performed until then, Swiss costs of comparable treatments were used where applicable (e.g. replantation of the hand for operation and rehabilitation, solid organ transplantation for donor costs). For prosthetic treatment, empirical costs were used from the cost databases of the accident insurer, Suva.

Costs were calculated for the year 2012 in Swiss francs (CHF). An average exchange rate of CHF 1.21

for 1 EUR was used for the conversion into Euros (Schweizerische Nationalbank, 2014). A discount rate of 3.25% was applied and the time horizon of the cost model was a life-time view. The perspective was the accident insurer. Since the accident insurer in Switzerland covers medical costs as well as loss of working time, direct costs and indirect costs for production losses (until retirement age of 65) were calculated. Average expected costs were calculated for the model patient, including costs of complications that were multiplied by their likelihood of occurrence. For an accurate estimate of the long-term effects, however, the number of existing cases was too small and the published observation time too short. Thus, assumptions had to be made based upon the existing data on hand transplantation as well as on solid organ transplantation. For the calculation of costs, complications were then divided into three groups; low, medium and high cost. To account for uncertainty, a sensitivity analysis was performed.

Information on ethical, legal and organizational issues was derived from expert interviews and the literature. The findings were then validated by the experts.

Results

Literature search

Two different literature searches were performed; one on hand transplantation and one on hand prosthesis fitting. In the broader search for hand transplantation, 507 references were screened. Eleven references were included after assessment of the full text and evaluated (Cavadas et al., 2011; Dubernard et al., 2003; Hautz et al., 2011; Hodges et al., 2000; Jablecki, 2011; Jones et al., 2000; Kaufman and Breidenbach, 2011; Ninkovic et al., 2011; Petruzzo and Dubernard, 2011; Petruzzo et al., 2008, 2010). The literature on hand transplantation typically includes case reports. We found no primary studies or reviews. The scoping search on hand prosthetics fitting yielded 47 references for more detailed screening. Finally, the information from seven references was evaluated (Datta et al., 2004; Davidson, 2004; Gabl and Kropfl, 2008; Graham et al., 1998; Leithner et al., 2008; Ostlie et al., 2011; Pinzur et al., 1994).

Use of health technology

Hand transplantation is the replacement of a missing hand of a hand-amputee through a donor hand. The goal is the recovery of functionality, sensitivity and the natural body image. With very few exceptions, hand transplantations have been performed only on

forearm amputees. According to experts, hand transplantation is particularly appropriate for bilateral amputees. Unilateral hand transplantation is controversial because of the unfavourable risk-benefit ratio due to the complications resulting from immunosuppression. Nevertheless, the majority of patients involved in hand transplantations to date are unilateral hand amputees (IRHCTT, 2012).

A potential recipient must be suitable medically, psychologically and socially. Very few patients are eligible for hand transplantation. The procedure has been performed in a number of centres worldwide, with no centre having done more than about six patients.

Effectiveness

For the assessment of the effectiveness of hand transplantation the following outcome criteria are the most relevant: functionality (DASH score or Carroll test) (Carroll, 1965; DASH Score, 2014) health-related quality of life (HRQL) (e.g. measured with EQ-5D or SF36) and loss of the transplanted hand (NICE, 2010).

Functionality includes mobility and sensitivity. The recovery of sensitivity is the main difference and the main advantage of hand transplantation in comparison with a prosthesis. In addition, the transplanted hand is usable continuously unlike the prosthesis. Of the 31 patients that underwent unilateral and bilateral transplantations that were reported in the International Registry on Hand and Tissue Transplantation until 2010, all 31 acquired the important protective sensitivity, 30 acquired patients tactile sensitivity and 28 patients discriminative sensitivity (Petruzzo et al., 2010).

The mean DASH score of the 31 registered hand transplanted patients in the register was 37.9 points after 1 year (Petruzzo et al., 2010). (Scaling was ranked from 0 indicating least disability to 100 indicating most disability.) Compared with a Norwegian study with 194 long-term prosthesis wearers (186 unilateral and eight bilateral) with a mean DASH score of 22.7 points (95% CI: 20.3–25.0), hand transplanted patients had less good function.

The measurement of HRQL is designed to show the contribution of a transplanted hand to the well-being in the daily life of an individual, physiologically, psychologically and socially. Unfortunately, no data (e.g. using SF36 or EQ-5D) has been found in the published literature.

In the literature, the information on the ability of transplanted patients to work is sparse. According to the IRHCTT, eight out of 12 patients could work again after transplantation (Petruzzo et al., 2008). A study on hand prosthesis found that 11 out of 15

people were still working after an amputation (Pinzur et al., 1994).

Transplantation has many similarities to a replantation. A study shows, however, that about 80% of the patients that had distal forearm replantation were able to work again, which is a higher proportion than for transplantation (Meyer, 2003). This is surprising because there are additional surgical difficulties in replantation depending on the type of injury. Unfortunately information on the level of employment is missing. The best comparable situation with transplantation is a replantation in patients with so-called 'guillotine-type amputation' (Meyer, 2003). In those cases, there are no other injuries to the hand or arm, and therefore, they are similar to transplantation from a surgical point of view. We tried to find Swiss data for such patients. Unfortunately we could only retrieve four patient records from the years 1974 to 1988. The average disability degree was 17%. Therefore, in the absence of better data, we used this value for the calculation of the pension amount for our model patient with transplantation. Based on 12 patients from 1996 to 2005, patients supplied with prostheses have an average invalidity of 45%.

Of the 31 registered uni- or bilaterally hand transplanted patients until 2010, only three suffered re-amputation (Petruzzo et al., 2010). The reasons were an infection after 45 days, intimal hyperplasia of the arteries after 9 weeks and non-compliance with the immunosuppressant.

Safety

Possible complications due to hand transplantation can be divided into three categories: (A) surgery/ anaesthesia, (B) transplantation of foreign tissue (e.g. graft versus host reaction) and (C) immunosuppressive therapy (e.g. infections). Surgery itself is associated with risks. The operation is very similar to a hand replantation. However, experts emphasise that, from a surgical point of view, replantation is even more demanding than transplantation due to damaged tissue that cannot be replaced.

In an allotransplantation there is always the risk of acute or chronic rejection. A total of 85% of reported hand-transplanted patients have experienced at least one acute rejection episode (Petruzzo et al., 2010). Most patients also experience some minor as well as some serious and potentially life-shortening complications because of the lifelong administration of immunosuppressive drugs. The most common complications are cytomegalovirus infection, bacterial infection and hyperglycemia.

In contrast to hand transplantation, only minor complications arise when wearing a hand prosthesis.

These complications include bruising, contact allergies (often related to sweating) and shoulder problems due to heavy prosthetics (Dudkiewicz et al., 2004).

Economic aspects

The costs of hand transplantation for preliminary examinations, surgery, rehabilitation and treatment of complications are significant and exceed the cost of care with a prosthesis. Table 1 shows the different cost components according to the cost model. The total cost for our model patient with hand transplantation over the remaining life span is CHF 977,000 (EUR 810,500). The lifetime cost for treatment with a prosthesis is CHF 631,900 (EUR 524,300). The difference of CHF 345,100 (EUR 286,200) arises from two components. The direct costs of the medical treatment are CHF 528,600 (EUR 438,500) higher for transplantation, with costs of immunosuppression alone accounting for almost 40% of the difference. Due to the assumed lower degree of invalidity of the transplanted patient, the expected costs due to reduced earnings capacity are lower by CHF 183,500 (EUR 152,300).

A sensitivity analysis was conducted for critical parameters, such as the difference in life expectancy and the discount rate. Table 2 shows how the difference in costs between conservative treatment and transplantation varies with different values of these parameters. The discount rate has a significant effect on the result because a large share of the costs is caused by immunosuppression in the future. Additional economic costs for transplantation decreases if the expected difference in life expectancy increases. If the life shortening effect of immunosuppression is more severe, future costs for immunosuppression and pension payments will be reduced. However, we need to keep in mind that in a cost-utility setting this would also lead to a reduction in the number of quality-adjusted life years gained for transplantation. It is plausible to assume that a reduction in life expectancy would have a negative effect on a measure of cost-utility for transplantation (i.e. cost per quality-adjusted life year (QALY) gained), even if it leads to lower additional costs of transplantation.

A cost-utility analysis could not be performed because of lack of utility values (which would be necessary for the calculation of QALYs). An American study by Chung et al. (2010) reports utility values for uni- and bilateral hand transplantation that were determined in a survey of 100 (non-amputated) medical students. Those utility values were then used in that study for calculations of QALYs, which are often used in health economic analysis. The study concluded that the gain

Table 1. Costs of hand transplantation versus prosthesis.

Direct cost		Indirect cost		Total			
<i>Hand transplantation</i>							
A. Treatment first 5 years	1. Assessment and preparation	2. Removal of organ and surgery	3. Examinations	4. Complications	Total medical cost	B. Reduced earnings capacity	Total
CHF 83,300	CHF 19,500	CHF 42,700	3.1. Follow-up CHF 127,100 3.2. Immunosuppression CHF 194,200 3.3. Rehabilitation CHF 43,900	CHF 180,000	CHF 690,700	CHF 286,300	CHF 977,000
<i>Treatment with prosthesis</i>							
Medical cost (1–4)					Total medical cost	B. Reduced earnings capacity	Total
CHF 162,100					CHF 162,100	CHF 469,800	CHF 631,900
Thereof:							
Cost years 1–5:		Cost per subsequent year:					
CHF 83,300		CHF 3900			Direct cost	Indirect cost	Total
					CHF 528,600	-CHF 183,500	CHF 345,100
Difference in cost							

^aCost for removal of organ and transport, as well as surgery and the part of inpatient treatment that is analogous to replantation. Cost of preliminary examinations are part of block number 1, costs specific to transplantation (tests and medications) are part of block 3.1 and 3.2. Bold entries highlight overall results with and without indirect costs.

Table 2. Sensitivity analysis.

Discount rate	Difference in cost
0	CHF 641,900
0.01	CHF 522,600
0.02	CHF 431,100
0.0325	CHF 345,100
Difference in life expectancy	
0	CHF 363,100
1	CHF 357,300
2	CHF 351,200
3	CHF 345,100
4	CHF 338,700
5	CHF 332,100
6	CHF 325,300
7	CHF 318,300

Bold entries show base case results

in quality of life due to hand transplantation in comparison with hand prosthesis can probably justify the considerable costs (in medical and economic terms) for bilateral amputees. Whether or not the high costs for hand transplantation can be justified depends on the expected utility gain of transplantation in comparison with prosthesis. This is subject to considerable uncertainty due to a lack of studies on this subject.

The number of cases in Switzerland would be very low in the near future, which renders the budget impact almost negligible. According to the Swiss medical statistic of hospitals (Bundesamt für Statistik, 2010), there were 201 cases of hand amputations in Switzerland in the 12 years from 1998 to 2009. No case of bilateral amputation was reported. After the deduction of 23 hand-replanted patients, a total of 178 potential cases remain for transplantation, which results in an average of 15 patients per year. According to expert opinion, fewer than 10% of all amputated cases qualify for hand transplantation. Thus, only about one patient per year would be eligible for hand transplantation in Switzerland.

In summary, individual additional costs for hand transplantation are very high. The low expected number of cases means a low potential budget impact for the system. The cost-effectiveness of the procedure is unknown due to a lack of reliable information on the effect of transplantation on quality of life. Better cost-effectiveness can be expected for bilaterally amputated patients compared with unilaterally amputated because of a higher expected gain in quality of life.

In this section, all the costs for the individual procedure were calculated that are incurred by accident insurance. The costs for the setup of a hand transplantation programme, typically including research

costs, were not calculated. Expert information suggests that such costs might be significant.

Legal aspects

From a legal perspective, hand transplantation is possible in Switzerland. One controversial issue was, whether the hand is defined as an 'organ' or as a 'tissue' in a legal sense. In the Swiss context, the hand falls under the definition of an 'organ', although internationally it is typically defined as a 'composite tissue'. This has legal consequences, because human organs have to follow a stricter government regulation than human tissues. One such regulation is that centres that want to perform organ transplantation need an explicit government authorization, which is not the case for tissue transplants. Another is that the allocation of organs to recipients must be centrally organized by a government agency. In the case of hand transplantation, no shortage of organs is expected in contrast to solid organs, due to the fact that very few patients are eligible for the procedure.

Ethical aspects

Following the medical ethicists Beauchamp and Childress (2009), in all medical treatments several moral principals have to be applied: (1) the principle of respect for autonomy; (2) the principle of non-maleficence; (3) the principle of beneficence; and (4) the principle of distributive justice. The HTA applied these moral principles to hand transplantation and it concluded that there are no ethical problems that could not be solved if the corresponding moral principles are applied.

Organizational aspects

A final important aspect is the organizational domain. Hand transplantation is a highly specialized procedure that requires a highly co-ordinated interplay of different medical disciplines. Switzerland is a small country and the expected number of hand transplant procedures is on average one or less per year. Therefore, the building of, at most, one centre could be justified. Collaboration with an already established centre abroad should be examined. In that case, further organizational and legal challenges would have to be overcome.

Discussion

Hand transplantations have been performed worldwide for over 15 years. Nevertheless, this method of treatment cannot be described as routine. The number

of cases remains very small and no centre in any country so far has carried out more than half a dozen such operations. As long as the negative effects of immunosuppression cannot be minimized, hand transplantation will remain controversial. Furthermore, hand transplantation causes significantly higher costs compared with hand prosthesis. The calculated cost differences of a transplanted 35-year-old model patient compared with prosthesis is CHF 345,100 (EUR 286,200) over the expected remaining lifetime. This amount results from the additional direct treatment costs of CHF 528,600 (EUR 438,500) minus the avoided indirect costs (reduction in production losses) of CHF 183,500 (EUR 152,300). The expected gain in quality of life would have to be large to justify the costs. These gains are likely to be much higher in bilaterally amputated patients compared with unilaterally amputated patients. Due to the expected small number of eligible patients (about one case per year), the overall budget impact should be minimal. Ethical, legal and organizational issues are considerable, but they could be handled if dealt with appropriately.

The HTA in the context of the funding decision

It is typically not the purpose of an HTA report to make a recommendation for a decision, but only to report all the relevant facts and to answer the scientific questions that were posed. Therefore, the report went to an HTA expert within the secretariat of the committee MTK UVG for an appraisal. That expert valued the HTA report and made a recommendation in an appraisal document for the attention of the committee. The recommendation of that appraisal was not to fund hand transplantation for ethical reasons, because of the considerable side effects of immunosuppression in relation to the relatively limited health gains, particularly for unilateral amputees. The deciding body (MTK UVG) carefully considered all the facts and decided that hand transplantation should not be funded in the context of the compulsory Swiss accident insurance scheme. Following the recommendation of the appraisal document, the committee valued the side effects of lifelong immunosuppression and health damage higher than the possible sensory and functional benefits.

Methodological strengths and limitations of the HTA

To our knowledge this is the first systematic multidisciplinary assessment (full HTA) of hand transplantation in Europe. The study provides a detailed description of

the anticipated cost of hand transplantation compared with prosthesis in forearm amputees from the perspective of accident insurance in Switzerland. Our systematic and multidisciplinary analysis with the methodology of HTA has been shown to be a useful tool for decision-making on reimbursement.

The HTA has some limitations. First, the published scientific literature has been sparse, since there are still few cases worldwide. It is dominated by case reports and opinions of experts from transplantation centres. Therefore the results run the risk of bias. Frequently, the same patients are described in various publications. Soon after our literature search, a systematic review was published with paired pre- and post-transplantation DASH scores for ten patients. They found a higher DASH score of 43.39 (SD26.48) after transplantation than in the 31 patients in the IRHCTT who had a mean DASH score of 37.9 (Landin et al., 2012). A higher DASH score indicates a greater handicap. Second, there is no published data on the important issue of general HRQL. HRQL is a highly important patient-related outcome measure. It would be needed to calculate a meaningful incremental cost-effectiveness ratio between hand transplantation and hand prosthesis. Third, it should again be emphasized that the cost calculations of this study are based on model assumptions. The data sources and calculation methods were consistent with best international practice in hand transplantation (to calculate quantities) and the best available Swiss cost data. We had to make strong assumptions on reduced work capacity of hand transplanted people based on very little information. The international data is sparse. Although the model calculation is as accurate as possible, the individual case of a single future patient may deviate from it significantly. Finally, we only compared hand transplantation with conventional prostheses. We did not include the latest developments in robotic prostheses. Whether the future of treatment of hand amputation lies in hand transplantation or high-tech hand prosthesis remains to be seen. The improvement of functionality and even gaining some sort of sensitivity could be a breakthrough for prosthesis. On the other hand, the development of less toxic immunosuppressive agents or the development of methods to induce immunological-tolerance could give hand transplantation a boost.

Implications for future research

The number of cases worldwide remains low. The IRHCTT remains the best database to date. However, the data items collected so far are limited. Additional collection of quality of life data (measured by a standard quality of life instruments such as the EQ-5D)

would be a useful additional outcome measure as well as data on resource consumption. Ideally, the same outcome data for patients with robotic hand prosthesis would be collected. This would allow a comparison of costs and consequences of both methods which would lead to better data for future decision-making by health care payers.

Conclusions

Hand transplantation remains a controversial method of treatment, with critical medical, economic, ethical, legal and political issues. The main problem remains the lifelong immunosuppression that causes high human, medical and economic costs in relation to a presumably marginal benefit for the patient. The HTA methodology proved to be a useful tool in the process of decision-making in the context of the Swiss accident insurance.

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Conflict of interests

None declared.

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