Technoleg Iechyd Cymru
Health Technology Wales

Topic Exploration Report

Topic explorations are designed to provide a high-level briefing on new topics submitted for consideration by Health Technology Wales. The main objectives of this report are to:

- Determine the quantity of evidence available for a technology of interest.
- Identify any gaps in the evidence.
- Inform decisions on topics that warrant fuller assessment by Health Technology Wales (HTW).

Topic exploration report number:	TER432
Topic:	Gracilis free-functioning muscle transfer (FFMT) to restore upper limb function in brachial plexus injury
Summary of findings:	The National Institute for Health and Care Excellence (NICE) published an Interventional procedures guidance (IPG687) in March 2021. The search covered the period from their start to 26 October 2020. Health Technology Wales researchers searched for additional clinical evidence published since the search date, and any additional cost effectiveness data with no search limits. Since the IPG, HTW researchers identified three systematic reviews, one meta-analysis and one additional observational study. Outcomes include the Medical Research Council (MRC) strength scores, range of motion (ROM) scores, and the Disabilities of the Arm, Shoulder, and Hand (DASH) scores. Overall, outcomes favour free functioning gracilis muscle transfer. DASH scores and strength scores were reported as better with FFMT when compared to non-FFMT. Additionally, procedural failure rates were lower with FFMT when compared with non-FFMT. Apart from procedural failures, the evidence report low adverse events. Although for most outcomes, the statistical significance was not reported and variables such as the type of intervention (i.e., single of double muscle transfer) and the type of comparator varied across the studies identified in the systematic reviews. HTW researchers identified a cost-effectiveness analysis of nerve transfer versus muscle transfer to restore elbow flexion after pan-brachial plexus injury in the US where the results included several treatment strategies, including FFMT. It is s unclear at this stage whether these findings would be generalisable to UK. We did not identify any relevant ongoing studies that were due for completion within the next year.

Introduction and aims

Brachial plexus injuries are caused by damage to the nerves in the arm and shoulder. This can be caused by trauma, tumours, and inflammation and when severe, they most commonly incur in the context of road traffic incidents. Severe nerve damage can lead to paralysis of an upper limb, with a loss of function and sensation, and severe pain. Current treatments include medicines to treat pain and conservative care (such as physiotherapy). For some people, surgical procedures are needed to restore function. These include direct suture, nerve grafts, nerve transfer, tendon transfer and free-functioning muscle transfer (FFMT).

In FFMT, a functioning gracilis muscle, with its own nerve and blood supply, is dissected from the inner thigh under general anaesthesia. The gracilis muscle is then transferred and joined to the prepared recipient site of the upper limb and the gracilis muscle's nerve is connected to a functioning nerve in the arm. The intended benefit of the procedure is usually to reconstruct a single function, such as elbow flexion.

HTW researchers searched for any evidence on the clinical and cost-effectiveness of gracilis free-functioning muscle transfer (FFMT) to restore upper limb function in brachial plexus injury. The IPG produced by NICE formed the basis of this topic exploration report and thus, Health Technology Wales researchers searched for additional clinical evidence published since the search date, and any additional cost effectiveness data with no search limits.

Evidence overview

Guidance

The IPG (NICE 2021) reports that there are well-recognised complications documented within evidence on the safety of gracilis FFMT to restore upper limb function in brachial plexus injury. Complications included but not limited to flap failure or re-exploration, infection, and thrombosis., However, the evidence on its efficacy is adequate to support the use of this procedure provided that standard arrangements are in place for clinical governance, consent, and audit. These conclusions were based off two systematic reviews, four non-randomised comparative studies and four case series studies. Where reported, three studies were conducted in the US, one in Japan, two in Brazil, one in the Philippines and one in Iran. The most common muscle was the gracilis, although the evidence base did include other muscle types. The committee noted that this procedure can be done as a single or double free-functioning gracilis transfer, although the evidence suggests a double transfer may be more effective.

Evidence reviews

Three systematic reviews and one meta-analysis have been identified since the IPG search. However, these reviews included studies which were a mix of prospective and retrospective observational studies. Eight out of 10 studies in the IPG are also referenced across these subsequent reviews identified since the search. The donor muscle varied vary across studies, although the gracilis muscle was mostly treated. The comparator also varied across studies and the intervention varied between single and double FFMT.

One systematic review, (Griepp et al. 2022) and one meta-analysis, (Scollan et al. 2020) compared outcomes of gracilis FFMT with non-free muscle transfers (non-FFMT) in restoring elbow flexion. Griepp et al. (2022) identified 46 observational studies that were either prospective or retrospective

studies where single nerve transfers made up the bulk of non-FFMT procedures. Scollan et al. (2020) included six retrospective observational studies in their meta-analysis.

Reed et al. (2022) conducted a systematic review (based in the UK) of 39 observational studies on FFMT for upper limb paralysis, where the most common muscle was the gracilis (91.5% of cases) and the most common cause of paralysis was brachial plexus injury. The comparators used across the identified observational studies varied. An additional systematic review, (Oliver et al. 2020) compared FFMT innervated by either intercostal nerve (ICN) or spinal accessory nerve (SAN) grafts for brachial plexus injury to compare postoperative elbow flexion outcomes.

DASH scores

DASH score is a validated method of evaluating arm functions based on 30 questions, with scores ranging from 0 (no disability) to 100 (severe disability). Griepp et al. (2022), in their pooled analysis found that the overall DASH scores for gracilis FFMT cases were lower than Oberlin nerve fascicle and single nerve cases. Scollan et al. (2020) pooled the mean DASH scores across studies and found that scores improved in the FFMT group when compared to non-FFMT, but this outcome not statistically significant, with a mean difference of 4.19 ($p = 0.22$). Reed et al. (2022) reported DASH scores from 39 observational studies, although the scores were not pooled in any statistical analysis.

Failure rates

The MRC grading system is used to measure postoperative strength graded from 0-5. Failure is defined as a score of less than three. A grade of three is generally considered the minimal postoperative strength to be considered a successful procedure.

In Griepp et al. (2022), FFMT were shown to have higher MRC strength scores than non-FFMT. The pooled mean MRC of all FFMT procedures was 3.40 compared to 2.99 for all non-FFMT procedures, although the statistical significance of this outcome was not reported In Griepp et al. (2022), procedure failure occurred in 18.4% of gracilis FFMT compared to 25.4% of non-FFMT. Scollan et al. (2020) found that the gracilis FFMT group had significantly lower odds of failure than the non-FFMT with an odds ratio value of 0.36 ($p = 0.002$). Scollan et al. (2020) reported in their meta-analysis that the FFMT group had a slightly larger mean difference of 0.02 in strength than the non-FFMT group, although this difference was not statistically significant with heterogeneity value of 72%, suggesting a high level of variance between the studies.

Reed et al. (2022) reported that 47.6% of FFMTs had a post-operative MRC grade of less than 4 and 18.1% of cases had an MRC of less than 3. However, the MRC scores were not pooled in any statistical analysis, neither were they compared with other treatment options of non-FFMT. Oliver et al. (2020) found that the mean success rates of FFMTs innervated by ICNs and SANs were 64.1 and 65.4%, respectively, although this study did not compare FFMT with non-FFMT or other treatment options.

ROM scores

ROM is the measurement of the amount of movement around a specific joint or body part. In context, this relates to elbow flexion. Scollan et al. (2020) found that studies had conflicting results regarding which treatment group had a greater ROM score, and there was no statistically significant difference between the FFMT and non-FFMT group in their meta-analysis. Griepp et al. (2022) reported ROM outcomes from 16 observational studies, although the outcomes were not pooled in any statistical analysis. In Griepp et al. (2022) no studies involving double nerve transfers reported ROM mean or

range values. The other two systematic reviews (Oliver et al. 2020, Reed et al. 2022) did not provide pooled ROM outcomes of FFMT when compared with non-FFMT.

Adverse events

The number of adverse events reported in the IPG evidence overview consisted of flap failure, infection reports, recipient site complications and donor site complications. Professional experts as part of the IPG did not list any anecdotal adverse events and theoretical adverse events. Apart from procedural failures, the number of adverse events reported in the systematic reviews identified since the IPG were low.

Individual studies

One additional retrospective non-comparative observational study of 160 participants in the US was identified since the IPG search. Hinchcliff et al. (2022) reported on the factors impacting the success of gracilis FFMT for elbow flexion in brachial plexus reconstruction with a minimum 2-year follow-up. Outcomes included DASH scores, MRC scores, and visual analogue scale pain scores. DASH scores improved from 45.7 to 38.8 and visual analogue scales also decreased. Additionally, 56.5% of patients achieved MRC grade three or higher, and 37.7% achieved grade four or higher. However, these outcomes were not statistically significant, and were not compared to other treatment options for brachial plexus injury.

Economic evidence

We identified a cost-effectiveness analysis of nerve transfer versus muscle transfer to restore elbow flexion after pan–brachial plexus injury in the US (Wali et al. 2017). The results included several treatment strategies including transfer of spinal accessory nerve (SAN) fascicles, intercostal nerve (ICN) fascicles, and gracilis FFMT. A Monte Carlo probabilistic sensitivity analysis demonstrated that at a willingness-to-pay of $50,000/QALY gained, SAN transfer dominated in 88.5% of iterations, FFMT dominated in 7.5% of iterations, and ICN dominated in 3.5% of iterations. The base case model demonstrated a lifetime QALYs of 22.45 in the SAN group, 22.0 in the ICN group, and 22.3 in the FFMT group. However, it is unclear at this stage whether these findings from a US perspective would be generalisable to the UK.

Areas of uncertainty

- There is some overlap in the included observational studies across the systematic reviews and the guidance produced by NICE.
- There is some uncertainty regarding the statistical significance of some outcomes.
- If this topic were to proceed to a fuller appraisal, consideration would need to be given to what comparators would be most appropriate.
- It is unclear at this stage how the US cost-effectiveness analysis would translate to cost-savings for the health system in the UK.

Literature search results

Health technology assessments and guidance
NICE. (2021). Free-functioning gracilis transfer to restore upper limb function in brachial plexus injury. Interventional procedures guidance [IPG687]. National Institute for Health and Care Excellence. Available at: https://www.nice.org.uk/guidance/ipg687 [Accessed 14 November 2022].
Evidence reviews and economic evaluations
Griepp DW, Shah NV, Scollan JP, et al. (2022). Outcomes of gracilis free-flap muscle transfers and non-free-flap procedures for restoration of elbow flexion: A systematic review. J Plast Reconstr Aesthet Surg. 75(8): 2625-36. doi: 10.1016/j.bjps.2022.04.025. Available at: https://pubmed.ncbi.nlm.nih.gov/35644885/ Oliver JD, Beal C, Graham EM, et al. (2020). Functioning Free Muscle Transfer for Brachial Plexus Injury: A Systematic Review and Pooled Analysis Comparing Functional Outcomes of Intercostal Nerve and Spinal Accessory Nerve Grafts. J Reconstr Microsurg. 36(8): 567-71. doi: 10.1055/s-0040-1713147. Available at: https://pubmed.ncbi.nlm.nih.gov/32526776/ Reed AJ, Claireaux HA, Wormald JC, et al. (2022). Free functional muscle transfer for upper limb paralysis - A systematic review. J Plast Reconstr Aesthet Surg. 75(3): 1001-17. doi: 10.1016/j.bjps.2021.09.038. Available at: https://pubmed.ncbi.nlm.nih.gov/34986998/ Scollan JP, Newman JM, Shah NV, et al. (2020). Free Gracilis Muscle Transfers Compared with Nonfree Muscle Flaps for Reanimation of Elbow Flexion: A Meta-Analysis. J Hand Microsurg. 12(1): 37-42. doi: 10.1055/s-0039-1697064. Available at: https://pubmed.ncbi.nlm.nih.gov/32280180/ Wali AR, Santiago-Dieppa DR, Brown JM, et al. (2017). Nerve transfer versus muscle transfer to restore elbow flexion after pan–brachial plexus injury: a cost-effectiveness analysis. Neurosurgical Focus FOC. 43(1): E4. doi: 10.3171/2017.4.FOCUS17112. Available at: https://thejns.org/focus/view/journals/neurosurg-focus/43/1/article-pE4.xml
Individual studies
Hinchcliff KM, Kircher MF, Bishop AT, et al. (2022). Factors Impacting the Success of Free Functioning Gracilis Muscle Transfer for Elbow Flexion in Brachial Plexus Reconstruction. Plast Reconstr Surg. 149(5): 921e-9e. doi: 10.1097/prs.0000000000009036. Available at: https://pubmed.ncbi.nlm.nih.gov/35271536/
Ongoing research
No evidence identified

Date of search:	November 2022
Concepts used:	gracilis transfer; brachial plexus injury; free-functioning gracilis transfer; cost.