FUNCTIONAL OUTCOMES OF FREE MUSCLE TRANSFER FOLLOWING ONCOLOGICAL RESECTION IN EXTREMITY SARCOMA: A COMPARISON STUDY BETWEEN NEUROVASCULARISED AND NON NEUROVASCULARISED FLAPS

DR RAGNILD ANAK REDIT

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LIST OF SYMBOLS, ABBREVIATIONS AND ACRONYMS

Abbreviations	Name
MSTS	Musculoskeletal Tumour Society
LEFS	Lower Extremity Functional Scale
QuickDASH	Quick Disabilities of the Arm, Shoulder and Hand
MRC	Medical Research Council
ROM	Range of motion
GCT	Giant cell tumour
CT	Computerised tomography
MRI	Magnetic resonance imaging
Et al.	Et alia
AJCC	American Joint Committee on Cancer
HUSM	Hospital Universiti Sains Malaysia
OORU	Orthopaedic Oncology and Reconstructive Unit
SD	Standard deviation
IQR	Inter quartile range

ABSTRAK

Pengenalan

Pembedahan memelihara anggota kaki dan tangan dengan rawatan adjuvant merupakan rawatan pilihan untuk kanser sarcoma pada anggota kaki dan tangan. Pemindahan otot bebas selalunya disyorkan untuk membina semula defek selepas pembedahan onkologi dengan atau tanpa pemulihan fungsi.

Metodologi

Ini adalah satu kajian retrospektif kohort untuk menentukan dan membandingkan hasil fungsi anggota kaki tangan antara *neurovascularised* dan *non neurovascularised,* serta morbiditi pada tapak penderma otot untuk pesakit-pesakit yang telah menjalani pembedahan onkologi pada anggota kaki dan tangan. Hasil fungsi selepas pembedahan ditentukan berdasarkan pemeriksaan klinikal, termasuk kekuatan otot dan julat pergerakan anggota terlibat; dan soal selidik, termasuk *Musculoskeletal Tumour Society (MSTS) score, Lower Extremity Functional Scale (LEFS)* dan *QuickDASH (Disabilities of Arm, Shoulder and Hand) questionnaire*.

Keputusan

Sejumlah 16 pesakit (11 lelaki dan 5 perempuan) dengan median umur 33 tahun terlibat dalam kajian ini. Semua pesakit menghidapi kanser sarkoma yang melibatkan anggota kaki dan telah menjalankan pembedahan rekonstruktif dengan otot *latissimus dorsi*

flap. Secara keseluruhan, hasil fungsi adalah cemerlang ke sederhana (skor median MSTS 26 dan skor median LEFS 57), dengan kekuatan otot yang diganti sekurang-kurangnya M3 untuk semua kecuali 2 pesakit. Tiada perkaitan ketara dari segi hasil fungsi antara dua kumpulan *neurovascularised* dan *non neurovascularised flap*. Hanya 1 pesakit mengalami komplikasi minor pada tapak penderma otot (*seroma*) dan hasil fungsi tapak penderma otot adalah memuaskan.

Kesimpulan

Hasil fungsi pembedahan memelihara anggota kaki tangan adalah baik sehingga cemerlang, akan tetapi tiada perkaitan ketara antara jenis pemindahan otot bebas dalam pembedahan rekonstruktif selepas pembedahan onkologi. Morbiditi pada tapak penderma otot flap adalah memuaskan, tetapi tidak dapat diabaikan, dengan hampir tiada pengehadan dalam aktiviti-aktiviti harian.

ABSTRACT

Introduction

Wide margin surgery combined with adjuvant radiotherapy has become the mainstay of treatment in extremity sarcomas, even in large sarcomas. Free muscle transfers are usually indicated for reconstruction of major defect following massive oncological resection. Apart from soft tissue coverage, functional restoration is possible by motorising the recipient motor nerve of the muscle flap.

Methods

This was a retrospective cohort study to determine and compare the functional outcomes between neurovascularised and non neurovascularised flaps, as well as the donor site morbidity who had undergone free muscle transfer following oncological resection surgery for extremity sarcoma. Functional outcomes of the surgery were then determined based on clinical examination, including muscle power and range of motion (ROM) of the affected extremity; and questionnaires, including the Musculoskeletal Tumour Society (MSTS) score, Lower Extremity Functional Scale (LEFS) and QuickDASH (Disabilities of Arm, Shoulder and Hand) questionnaire.

Results

A total of 16 patients (11 males and 5 females) with a median age of the patients was 33 years old were recruited for this study. All the patients had lesions in the lower extremity

and were reconstructed with a free latissimus dorsi muscle flap. Overall functional outcome ranged from excellent to fair (median MSTS score of 26 and median LEFS score of 57), with muscle strength of replace muscle of at least M3 in all but 2 patients. There were no significant association in the functional outcomes between both neurovascularised and non neurovascularised groups. There was only 1 patient with minor donor site complication (seroma) and functional outcome of the donor site was acceptable.

Conclusion

The functional outcomes of limb salvage surgery are shown to be good to excellent, however there is no significant difference between the type of free muscle transfer in the reconstruction of the resected muscle compartment in our study. This result implied that functional neurovascularised muscle flap in major resection also achieved good functional outcome. Donor site morbidity for latissimus dorsi muscle harvest is acceptable, but not negligible with limited to no functional limitations in activities of daily living.

CHAPTER 1: BACKGROUND

1.1 Introduction / Problem Statement

Sarcomas are a heterogenous group of rare tumours that arise predominantly from the embryonic mesoderm. The term *sarcoma* refers to a tumour of connective tissue and derives from the Greek *sarcos* (flesh) and *sarkoma* (fleshy substance). The various sarcomas include bone sarcoma (osteosarcoma, chondrosarcoma), Ewing's sarcoma, peripheral primitive neuroectodermal tumours, and soft tissue sarcomas, which are the most frequent. (Skubitz and D'Adamo, 2007)(Spiguel, 2014)

Sarcomas account for over 20% of all paediatric solid malignant cancers and less than 1% of all adult solid malignant cancers. The vast majority of diagnosed sarcomas are soft tissue sarcomas, while malignant bone tumours make up just over 10% sarcomas. (Burningham et al., 2012)

According to the Malaysia National Cancer Registry Report in the year 2017, out of 110 965 cases of malignancy reported, only 1976 cases (~1%) comprise of bone and soft tissue sarcoma. (National Cancer Institute, 2019)

Sarcomas can occur anywhere in the body, but most originate in an extremity, in which 45% occur in the lower extremity and 15% occur in the upper extremity. The remaining cases occur in the trunk (15%), the retroperitoneum (15%), or the head and neck (10%). (Spiguel, 2014) Extremity sarcomas are most common in the thigh (50-60%).

In a local study by Wan Yuhana in 2017, sarcomas showed an overall median survival rate of 10 years with a 5-year survival rate of 58% in adults with extremity soft tissue

sarcoma. Pulmonary and distant (non pulmonary) metastases, and local recurrence were prognostic factors that significantly affect overall survival. (Yahaya et al., 2017)

Over the years, the surgical treatment of lower extremity sarcomas have evolved from limb amputation to limb salvage or preservation surgery with adjuvant treatments such as chemotherapy and radiotherapy given either preoperatively or postoperatively. (Muramatsu, et al., 2012)(Payne et al., 2013) In addition to better preservation of the majority of limb functions, it also provides greater psychological and physiological benefits.

In order to achieve adequate surgical margins, secondary huge soft tissue defects usually result in exposure of vital structures after tumour resection of extremity sarcoma. In these cases, it is frequently indicated for free tissue transfers for coverage of the critical structures, such as nerves and/or vasculature and can further facilitate healing when bone and tendon are exposed. (Agrawal et al., 2013) This in turn also reduces concern over ability to achieve wound closure, so complete resection can be pursued aggressively. (Grinsell, 2012) Free muscle transfers are generally the preferred option as it not only obliterates dead space and covers skin defect, but also produces a functionally useful limb.

Advantages of free functional muscle transfer is it provides adequate soft tissue coverage and simultaneous restoration of function of the affected extremity and joint. Performance of the salvaged limb generally shows significant improvement after recovery of the muscles, as the free neurovascularised muscle transfer can also provide active contraction. (Ihara, 1999)

Flap choice is made to minimise donor site morbidity and to maximise extremity function. Donor muscle used for reconstruction is selected based on muscle volume and size of overlying skin flap. With any free flap operations, complications may arise at the flap site,

donor site or systemically. The prevalence of donor site morbidity after free flaps ranges from 5.5% to 14.8%. (Classen and Ward, 2006)(Singh, 1999)

However, the success of surgical management cannot be assessed only by oncological and operative results, but must be balanced by consideration of functional outcomes. In order to accurately measure the functional status post oncological resection, a combination of reliable, valid and responsive instruments can be used. (Payne et al., 2013)(Innocenti et al., 2009)

1.2 Objectives

1.2.1 General Objective

To determine and compare the functional outcomes of neurovascularised and non neurovascularised free muscle transfer following oncological resection in extremity sarcoma

1.2.2 Specific Objectives

i. To determine mean of functional outcomes using the disease-specific scoring system – Musculoskeletal Tumour Society (MSTS) score

ii. To determine mean of the overall function using the Lower Extremity Functional Scale (LEFS) (for lower extremity) and QuickDASH (Quick Disabilities of the Arm, Shoulder and Hand) questionnaire (for upper extremity)

iii. To determine proportion of different muscle strength in the reconstructed compartment using the MRC scale

iv. To determine proportion of range of motion (ROM) of the joint(s) controlled totally or partially by the innervated flap

v. To determine prevalence of complications and function disabilities from donor site morbidity – using the QuickDASH questionnaire (Quick Disability of the Arm, Shoulder and Hand)

1.3 Research Questions

i. Does limb salvage surgery with neurovascularised and non neurovascularised free muscle transfer improve the functional outcome in extremity sarcoma patients?

ii. Is there a difference in functional outcomes between neurovascularised and non neurovascularised free muscle transfer following oncological resection in extremity sarcoma?

iii. What is the prevalence of complications and functional disabilities from the donor site morbidity?

CHAPTER 2: LITERATURE REVIEW

2.1 Extremity sarcoma

Sarcomas are one of the rarest type of malignancy, in which a majority arise from the extremities. Sarcomas present as painless, slow growing masses which usually does not give a huge impact on the patient's overall function or general health status. This is turn typically leads to delayed disease presentation and large tumour size, often with presence of pulmonary metastases. (Skubitz and D'Adamo, 2007b; Spiguel, 2014) Large tumour volume poses a challenge to the ablative surgeon in achieving adequate surgical margin as there is a possibility of anatomical and functional deficiencies. The risk for local recurrence is increased in patients with inadequate surgical margins, and subsequently a greater risk of metastasis. (Gutierrez et al., 2007)The standard treatment for extremity sarcoma with the advances of adjuvant therapy is limb salvage surgery. To achieve better functional and cosmetic outcomes during limb salvage surgery following oncological resection, there have been higher demand for more complex reconstructive options.

Conventional free muscle transfer (non neurovascularised) is a favourable option in that it can achieve stable wound closure and effective soft tissue coverage in a single stage, prevention of lymphoedema and thus decreasing the infection rate. On the other hand, free neurovascularised muscle transfer has the added advantage of restoring joint movement. (Muramatsu et al., 2012)

2.2 Staging of Sarcomas

Staging of a musculoskeletal tumour is based on the findings of the clinical examination and the results of imaging studies. Biopsy and histopathological evaluation are essential components of staging but should always be the final step. (Schmookler, 2004)

The American Joint Committee on Cancer (AJCC) is based on tumour grade, size, and presence and location of metastases. Staging systems for soft tissue sarcoma of the extremity using the American Joint Committee on Cancer (AJCC) 8th edition. (Amin et al., 2017)

T1: Tumour ≤ 5cm in greatest dimension

T2: Tumour > 5cm and ≤ 10cm in greatest dimension

T3: Tumour > 10cm and ≤ 15cm in greatest dimension

T4: Tumour > 15cm in greatest dimension

N0: No regional lymph node metastasis or unknown regional lymph node status

N1: Regional lymph node metastasis

M0: No distant metastasis

M1: Distant metastasis

Stage groups

Stage IA: T1; N0; M0; G1

Stage IB: T2, T3, T4; N0; M0; G1

Stage II: T1; N0; M0; G2/3

Stage IIIA: T2; N0; M0; G2/3

Stage IIIB: T3, T4; N0; M0; G2/3

Stage IV: Any T; N1; M0; any G

Any T; any N; M1; any G

2.3 Overview Management of Sarcomas

Previously, limb amputation was the only option offered to patients with sarcoma of the extremities. However, with the developments in microsurgical techniques, as well as in combination with chemotherapy and radiation therapy, it has allowed patients to undergo limb salvage surgery. The management of malignant bone and soft tissue sarcomas requires a multidisciplinary approach with an orthopaedic oncology surgeon, reconstructive surgeon, radiologist, pathologist and oncologist for best possible care. (Ismail, 2015)(Azadgoli et al., 2018) The current standard of care for this includes wide tumour excision with adjuvant or neoadjuvant therapy.

According to guidelines published by Grimer et al (Grimer et al., 2010), there are four categories of surgical margins that have been described based on histological findings:

i. Intralesional – margin runs through tumour and therefore tumour remains.
ii. Marginal – surgical plane run through pseudocapsule (reactive zone). The local recurrence rate is high because of tumour satellites in the reactive tissue.
iii. Wide – surgical plane is in normal tissue but in the same compartment as the tumour. The recurrence rate is low and is related only to skip lesions in the affected compartment.

iv. Radical – the tumour is removed including affected compartments and there is minimal risk of local recurrence.

The plastic and reconstructive surgeon plays a vital role in the management of sarcoma because of the prospective reconstructive benefits, while simultaneously not negatively impacting tumour safety, survival or complication rates. (Götzl et al., 2020) There are various options for reconstruction including primary wound closure, use of split thickness skin grafts, local/regionals flaps or the use of free flaps with microvascular anastomosis. Free muscle transfer is a favourable option in that it can achieve stable wound closure and effective soft tissue coverage in a single stage, prevention of lymphoedema and thus decreasing the infection rate, besides psychological and physiological benefits. (Wright et al., 2008)(Ihara, 1999)(Muramatsu et al., 2012)

2.4 Functional Evaluation of Reconstructive Procedures

2.4.1 Musculoskeletal Tumour Society (MSTS) Rating Scale

Musculoskeletal Tumour Society (MSTS) rating scale was developed and introduced in 1983, and subsequently modified in 1993 (Enneking, 1985). It is a disease specific instrument to evaluate the functional outcomes in patients with extremity tumours. It is a clinician-rated scale with six parameters, in which each item is rated on a scale of 0 – 5, with a maximum score of 30.

Pain, function, and emotional acceptance are measured for both upper and lower extremities. For the lower extremity, use of walking aids, gait and walking are evaluated. For upper extremity, hand positioning, dexterity, and lifting ability are evaluated. Function is then expressed as percentage of the maximum score.

Score	Pain	Function	Emotional	External support	Functional Independence	Gait	Percentage (%)
5	None	No restrictions	Motivated	None	Independent	Normal	100
4	Intermediate	Intermediate	Intermediate	Intermediate	Intermediate	Intermediate	80
3	Not disabling	Recreational limitation	Satisfied	Orthesis	Limited	Minimal alteration	60
2	Intermediate	Intermediate	Intermediate	Intermediate	Intermediate	Intermediate	40
1	Incapacitating	Partial limitation	Accepts	Cane/crutch	Home	Very altered	20
0	Extremely incapacitating	Total restriction	No support	Two crutches	Dependent	Difficult	0

Source: DOT-UFRJ, 2017.

Table 1 Musculoskeletal Tumour Society (MSTS) rating scale

Score	Hand positioning	Manual dexterity	Lifting ability
5	Unlimited	No limitations	Normal load
4	(Intermediate)	(Intermediate)	(Intermediate)
3	Not above shoulder	Loss of fine movements	Limited (minor load)
2	(Intermediate)	(Intermediate)	(Intermediate)
1	Not above waist	Cannot pinch	Helping only (cannot overcome gravity)
0	None	Cannot grasp	Cannot move

Table 1 Musculoskeletal Tumour Society (MSTS) rating scale

2.4.2 Lower Extremity Functional Scale (LEFS)

The lower extremity functional scale (LEFS) is a valid patient-rated outcome measure (PROM) for the measurement of lower extremity function. It was first developed by Binkley et al. (1999) in a group of patients with various musculoskeletal conditions. (Binkley et al., 1999)(Mohd Yunus et al., 2017) The objective of the LEFS is to measure patient's initial function, ongoing progress, and outcome for a wide range of lower extremity conditions. It is a questionnaire containing 20 questions about a person's ability to perform everyday tasks, in which each question is scored 0 to 4. The maximum score is 80.

(Circle one number on each line)

Activities	Extreme Difficulty or Unable to Perform Activity	Quite a Bit of Difficulty	Moderate Difficulty	A Little Bit of Difficulty	No Difficulty
a. Any of your usual work, housework, or school activities.	0	1	2	3	4
b. Your usual hobbies, recreational or sporting activities.	0	1	2	3	4
c. Getting into or out of the bath.	0	1	2	3	4
d. Walking between rooms.	0	1	2	3	4
e. Putting on your shoes or socks.	0	1	2	3	4
f. Squatting.	0	1	2	3	4
g. Lifting an object, like a bag of groceries from the floor.	0	1	2	3	4
h. Performing light activities around your home.	0	1	2	3	4
i. Performing heavy activities around your home.	0	1	2	3	4
j. Getting into or out of a car.	0	1	2	3	4
k. Walking 2 blocks.	0	1	2	3	4
l. Walking a mile.	0	1	2	3	4
m. Going up or down 10 stairs (about 1 flight of stairs).	0	1	2	3	4
n. Standing for 1 hour.	0	1	2	3	4
o. Sitting for 1 hour.	0	1	2	3	4
p. Running on even ground.	0	1	2	3	4
q. Running on uneven ground.	0	1	2	3	4
r. Making sharp turns while running fast.	0	1	2	3	4
s. Hopping.	0	1	2	3	4
t. Rolling over in bed.	0	1	2	3	4
Column Totals:					

SCORE: _____/80

Error (single measure): ±5 scale points
MDC: 9 scale points
MCID: 9 scale points

Table 2 Lower Extremity Functional Scale (LEFS)

2.4.3 QuickDASH (Disabilities of the Arm, Shoulder and Hand) questionnaire

The disabilities of the arm, shoulder and hand (DASH) questionnaire is a self-administered region-specific outcome instrument developed as a measure of self-rated upper extremity disability and symptoms. It consists of a 30-item disability/symptom scale in patients with any or several musculoskeletal disorders of the upper limb, scored 0 (no disability) to 100 (maximal disability). The QuickDASH questionnaire is a shortened version of the DASH Outcome Measure consisting of 11 items to measure physical function and symptoms in patients with any or multiple musculoskeletal disorders of the upper limb. It is scored in 2 components: the disability/symptom section (11 items, scored 1 – 5) and the optional high performance sport/music or work modules (4 items, scored 1 – 5).

It has two optional modules intended to measure symptoms and functions in athletes, performing artists and other workers whose jobs require a high degree of physical performance. These optional modules are scored separately.

QuickDASH

Please rate your ability to do the following activities in the last week by circling the number below the appropriate response.

	NO DIFFICULTY	MILD DIFFICULTY	MODERATE DIFFICULTY	SEVERE DIFFICULTY	UNABLE
1. Open a tight or new jar.	1	2	3	4	5
2. Do heavy household chores (e.g., wash walls, floors).	1	2	3	4	5
3. Carry a shopping bag or briefcase.	1	2	3	4	5
4. Wash your back.	1	2	3	4	5
5. Use a knife to cut food.	1	2	3	4	5
6. Recreational activities in which you take some force or impact through your arm, shoulder or hand (e.g., golf, hammering, tennis, etc.).	1	2	3	4	5

	NOT AT ALL	SLIGHTLY	MODERATELY	QUITE A BIT	EXTREMELY
7. During the past week, *to what extent* has your arm, shoulder or hand problem interfered with your normal social activities with family, friends, neighbours or groups?	1	2	3	4	5

	NOT LIMITED AT ALL	SLIGHTLY LIMITED	MODERATELY LIMITED	VERY LIMITED	UNABLE
8. During the past week, were you limited in your work or other regular daily activities as a result of your arm, shoulder or hand problem?	1	2	3	4	5

Please rate the severity of the following symptoms in the last week. *(circle number)*	NONE	MILD	MODERATE	SEVERE	EXTREME
9. Arm, shoulder or hand pain.	1	2	3	4	5
10. Tingling (pins and needles) in your arm, shoulder or hand.	1	2	3	4	5

	NO DIFFICULTY	MILD DIFFICULTY	MODERATE DIFFICULTY	SEVERE DIFFICULTY	SO MUCH DIFFICULTY THAT I CAN'T SLEEP
11. During the past week, how much difficulty have you had sleeping because of the pain in your arm, shoulder or hand? *(circle number)*	1	2	3	4	5

QuickDASH DISABILITY/SYMPTOM SCORE = $\left(\left[\frac{\text{sum of n responses}}{n}\right] - 1\right) \times 25$, where n is equal to the number of completed responses.

A QuickDASH score may not be calculated if there is greater than 1 missing item.

Table 3 QuickDASH questionnaire

QuickDASH

WORK MODULE (OPTIONAL)

The following questions ask about the impact of your arm, shoulder or hand problem on your ability to work (including homemaking if that is your main work role).

Please indicate what your job/work is: _____

❒ I do not work. (You may skip this section.)

Please circle the number that best describes your physical ability in the past week.

Did you have any difficulty:	NO DIFFICULTY	MILD DIFFICULTY	MODERATE DIFFICULTY	SEVERE DIFFICULTY	UNABLE
1. using your usual technique for your work?	1	2	3	4	5
2. doing your usual work because of arm, shoulder or hand pain?	1	2	3	4	5
3. doing your work as well as you would like?	1	2	3	4	5
4. spending your usual amount of time doing your work?	1	2	3	4	5

SPORTS/PERFORMING ARTS MODULE (OPTIONAL)

The following questions relate to the impact of your arm, shoulder or hand problem on playing *your musical instrument or sport or both*. If you play more than one sport or instrument (or play both), please answer with respect to that activity which is most important to you.

Please indicate the sport or instrument which is most important to you: _____

❑ I do not play a sport or an instrument. (You may skip this section.)

Please circle the number that best describes your physical ability in the past week.

Did you have any difficulty:	NO DIFFICULTY	MILD DIFFICULTY	MODERATE DIFFICULTY	SEVERE DIFFICULTY	UNABLE
1. using your usual technique for playing your instrument or sport?	1	2	3	4	5
2. playing your musical instrument or sport because of arm, shoulder or hand pain?	1	2	3	4	5
3. playing your musical instrument or sport as well as you would like?	1	2	3	4	5
4. spending your usual amount of time practising or playing your instrument or sport?	1	2	3	4	5

SCORING THE OPTIONAL MODULES: Add up assigned values for each response; divide by 4 (number of items); subtract 1; multiply by 25.
An optional module score may not be calculated if there are any missing items.

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Table 3 QuickDASH questionnaire

2.4.4 MRC (Medical Research Council) Manual Muscle Testing Scale

The MRC scale for muscle power/strength was first published by the Medical Research Council in 1943, in which an ordinal scale for muscle weakness was introduced.

- 0 No muscle activation
- 1 Trace muscle activation, such as a twitch, without achieving full range of motion
- 2 Muscle activation with gravity eliminated, achieving full range of motion
- 3 Muscle activation against gravity, full range of motion
- 4 Muscle activation against some resistance, full range of motion
- 5 Muscle activation against examiner's full resistance, full range of motion

Further adaptation was made to this scale after it was noted to lack sensitivity in the context of slight degrees of weakness. Therefore, Grades 4-, 4 and 4+ were introduced for movement against slight, moderate and strong resistance, respectively. (Compston, 2010)

2.4.5 Range of Motion (ROM) of the joints

The active range of motion of the joint(s) controlled totally or partially by the innervated flap. It will be measured with no outside force or assistance aiding in the movement using a goniometer.

Normal range of motion of joints assessed:

- Hip: extension 0 to 30 degrees, flexion 0 to 125 degrees, abduction 0 to 40 degrees, adduction 0 to 20 degrees, internal rotation 0 to 40 degrees, external rotation 0 to 50 degrees
- Knee: extension 0 degrees, flexion 120 to 0 degrees
- Ankle: plantar flexion 0 to 40 degrees, dorsiflexion 0 to 20 degrees
- Shoulder: extension 0 to 40 degrees, flexion 0 to 180 degrees, abduction 0 to 180 degrees, adduction 20 to 40 degrees, internal rotation 0 to 80 degrees, external rotation 0 to 90 degrees
- Elbow: extension 0 degrees, flexion 0 to 150 degrees

2.4.6 Donor site assessment

Donor site complications can be divided into major and minor complications. A major donor site complication was one that necessitated repeat surgery, while a minor donor site complication were those that resolved on its own or entailed negligible intervention. (Classen and Ward, 2006) Complications include infection, haematoma, seroma, wound dehiscence, and surgical scar requiring revision.

In addition to these complications, functional morbidity will also be assessed. The subjective donor site morbidity would be evaluated, including the impact on the activities of daily living.

2.5 Study Rationale

The standard of treatment for extremity sarcoma is evolving from limb amputation to limb salvage or preservation. The motivation for limb salvage, albeit to various degrees, has been propelled to gradually replacing limb amputation by various measurable outcomes. Besides better preservation of the majority of limb functions, it also provides greater overall psychological and physiological benefits in carefully selected patients.

To date, several studies have reported the functional outcomes of reconstruction of extremity sarcoma after neurovascularised and non neurovascularised free muscle transfer. However, owing to the rarity of the disease state and available multidisciplinary expertise to provide higher level care with regards to the subject matter there is still a paucity of adequate data that investigate and assess the functional outcomes of patients with extremity sarcoma who have underwent oncological resection and free muscle transfer – both in neurovascularised and non neurovascularised groups of patients.

Here, we aim to assess and compare the functional outcomes of these group of patients using validated scoring system and provide valuable data to shape the progress of management algorithms in these subsets of patients.

CHAPTER 3: METHODOLOGY

3.1 Research Design

This was a retrospective, cohort study involving all patients who had undergone neurovascularised and non neurovascularised free muscle transfer following oncological resection surgery for extremity sarcoma.

3.2 Study Location and Duration

i. Hospital Universiti Sains Malaysia (HUSM)

    a. Reconstructive Sciences Unit

    b. Orthopaedics Oncology and Reconstructive Unit

ii. The study was done to include patients who underwent surgery from January 1998 to June 2020.

3.3 Study Population and Sample

The study population of interest include all patients who were diagnosed with an extremity sarcoma that have undergone either neurovascularised or non neurovascularised free muscle transfer post oncological resection that had been referred to the Reconstructive Sciences Unit and Orthopaedics Oncology and Reconstructive Unit, HUSM.

3.4 Sampling Technique

Universal sampling method will be employed throughout the course of this study due to the limited number of patients who meet the inclusion criteria.

3.5 Inclusion Criteria

- Patients diagnosed with an extremity sarcoma
- Patients previously diagnosed who presented with local recurrence
- Patients who have undergone oncological resection and neurovascularised or non neurovascularised free muscle transfer
- At least 1 year of follow up in HUSM postoperatively

3.6 Exclusion Criteria

- Patients who presented with synchronous metastatic disease not undergoing oncological resection
- Patients who underwent simultaneous reconstruction with osseous flap
- Patients who were premorbidly immobilised
- Incomplete information in patient's medical record files
- Patients in which medical record files are no longer available

3.7 Sample Size Calculation

Objective 1

Objective: To determine mean of functional outcomes using the disease-specific scoring system – Musculoskeletal Tumour Society (MSTS) score

Method: We applied the Single Mean Estimation using Sample Size Calculator by Arifin, W. N. (2021) to estimate our sample size of the first objective. Details of the formula is listed below:

- Standard deviation of (MSTS) score (σ) = 5.30 (Schreiber et al., 2006)
- Z value based on 95% CI = 1.96
- Precision (± mean) = 3
- Number of sample size (n) = 12
- Drop-out rate = 10 %
- Final sample size (with 10% dropout) (n) = **14**

Objective 2

Objective: To determine mean of the overall function using the Lower Extremity Functional Scale (LEFS) (for lower extremity) and QuickDASH (Quick Disabilities of the Arm, Shoulder and Hand) questionnaire (for upper extremity)

For LEFS

Method: We applied the Single Mean Formula using Sample Size Calculator by Arifin, W. N. (2021) to estimate our sample size. Details of the formula is listed below:

- Standard deviation of LEFS score (σ) = 12.25 (*Grinsell et al, 2012*)
- Z value based on 95% CI = 1.96

- Precision (± mean) = 7
- Number of sample size (n) = 12
- Drop-out rate = 10 %
- Final sample size (with 10% dropout) (n) = **14**

For Quick DASH

Method: We applied the Single Mean Formula using Sample Size Calculator by Arifin, W. N. (2021) to estimate our sample size. Details of the formula is listed below:

- Standard deviation of DASH score (σ) = 15.52 (*Grinsell et al, 2012*)
- Z value based on 95% CI = 1.96
- Precision (± mean) = 7
- Number of sample size (n) = 19
- Drop-out rate = 10 %
- Final sample size (with 10% dropout) (n) = **22**

Objective 3

Objective: To determine mean of different muscle strength in the reconstructed compartment using the MRC scale.

Method: We applied the Single Proportion Formula using Sample Size Calculator by Arifin, W. N. (2021) to estimate our sample size. Details of the formula is listed below:

- Proportion of muscle strength category = (p)
- Z value based on 95% CI = 1.96
- Precision (± proportion) = 0.3
- Drop-out rate = 10 %

- Final sample size (with 10% dropout) = (n)

Variable	p	n	n+10 % drop out	Literature Review
M5	0.41	11	**13**	(*Grinsell et al, 2012*)
M4	0.36	10	12	(*Grinsell et al, 2012*)
M3	0.05	3	4	(*Grinsell et al, 2012*)

Objective 4

Objective: To determine proportion of range of motion (ROM) of the joint or joints controlled totally or partially by the innervated flap.

Method: We applied the Single Proportion Formula using Sample Size Calculator by Arifin, W. N. (2021) to estimate our sample size. Details of the formula is listed below:

- Proportion of range of motion (ROM) fully restored (p) = 0.64 (*Grinsell et al, 2012*)
- Z value based on 95% CI = 1.96
- Precision (± proportion) = 0.3
- Number of sample size (n) = 10
- Drop-out rate = 10 %
- Final sample size (with 10% dropout) (n) = **12**

Objective 5

Objective: To determine prevalence of complications and function disabilities from donor site morbidity

Method: We applied the Single Mean Formula using Sample Size Calculator by Arifin, W. N. (2021) to estimate our sample size of the first objective. Details of the formula is listed below:

- Proportion of patients with postoperative complications (p) = 0.163 (Kask et al., 2019)
- Z value based on 95% CI = 1.96
- Precision (± proportion) = 0.2
- Number of sample size (n) = 14
- Drop-out rate = 10 %
- Final sample size (with 10% dropout) (n) = **16**

Final Sample Size

The final total sample size for our study is **22 samples**.

3.8 Research Tools

Data will be collected from patient's medical record files from Unit Rekod Perubatan, HUSM and recorded in "Extremity Sarcoma Proforma".

Goniometer will be used to measure active range of motion of the joint(s) controlled totally or partially by the innervated flap.

3.9 Variable Definition

Free muscle transfer: flaps that includes muscle component supplied by a dominant vascular pedicle in which the donor and recipient sites are not close to one another

Neurovascularised flaps: flap that is harvested with its blood supply along with its accompanying nerve supply

Non-neurovascularised flaps: flap that is harvested with its blood supply without accompanying nerve supply

3.10 Data Collection

Patients' details will be traced from the operative census book of Reconstructive Sciences Unit and Department of Orthopaedics, HUSM. Patients' medical record files will be obtained from Unit Rekod Perubatan and reviewed. Data will be entered into the "Extremity Sarcoma Proforma". Photo documents (routine pre-operative, intraoperative, post-operative photos) will be obtained from Reconstructive Sciences Unit office and Department of Orthopaedics if available.

This research will be conducted on a voluntary basis in such a way they are free to participate or refuse to take part in the study after hearing a brief explanation about the study.

If they are willing to participate, a written informed consent will be obtained from the responders or the legal guardian prior to any data collection. Only after the informed consent has been obtained will the responders be briefed about the proforma and interview process and data collection.

Detailed explanation of the proforma will also be given to the participants to ensure the accuracy of the collected information.

3.11 Statistical Analysis

Data collected was entered and analysed using the Statistical Package for Social Science (SPSS) software version 26. All categorical data were presented in frequency and percentage, while the numerical data were presented in median and interquartile range due to non-normal distribution of data. Comparisons between two groups were made using the Fisher's exact test or the Mann-Whitney Test, as appropriate. The P level of less than 0.05 was considered statistically significant.

3.12 Confidentiality and Privacy

Each patient will be given an identifier based on the acronym of their name in the proforma that is filled and no other personal identification data i.e. (telephone number, identification number card) will be recorded. Therefore, no direct link can be made to the patient once the data has been collected from them through the proforma.

The proforma will then be kept in a secure location known only to the research team members. Once the data has been entered into the SPSS software, it will be presented as grouped data and will not identify the participants individually.