ULBS
Universitatea "Lucian Blaga" din Sibiu

INSTITUTE OF DOCTORAL STUDIES

DOCTORAL SCHOOL: **MEDICINE**

DOCTORAL THESIS – SUMMARY

Perforator flaps for reconstruction of soft tissue defects of the lower extremity: an experimental and clinical study.

PhD student:

Radu Olariu

Doctoral Advisor:

Prof. Dr. Dan Sabău

SIBIU 2021

TABLE OF CONTENTS THESIS

1.INTRODUCTION

Perforator flaps are a relatively new method of reconstructing soft tissue and soft tissue defects that has become widespread due to the minimal morbidity of the donor site. Perforating vessels are defined as vessels that pierce (perforate) a muscle or fascia to reach and vascularise a specific skin segment. The technical advance that has revolutionised the use of flaps on perforators is the ability to dissect these small blood vessels using microsurgical techniques and thus avoid sacrificing deep, potentially functionally important structures.

Although the use of flaps on perforators is expanding in clinical practice, the experimental data related to these flaps are relatively scarce. In particular in the case of pedicled, local, perforator-based flaps ("propeller" flaps, propeller flaps) experimental data are scarce and the recognised problems of partial necrosis have not been fully understood.

So far research in this area has focused on detecting the most powerful perforating vessels to vascularise the most extensive flaps, with no studies on the possibility of actively influencing blood flow through a given perforating vessel. There are also a limited number of studies examining the role of local, pedicled-based perforator flaps in covering traumatic lower limb defects.

Therefore, we set a dual objective in this study. On the one hand, we evaluated in an experimental model the effects of active changes in arterial flow and/or venous return pressure on the survival rate of perforator flaps. On the other hand, from a clinical point of view we performed a detailed analysis of the results of post-traumatic lower limb reconstructions with local pedicled perforator-based flaps used in the author's clinical unit.

2. THEORETICAL PART

2.1 History and concepts in lower limb reconstruction

The evolution of surgical therapy of traumatic lower limb injuries spans millennia of human history and has been significantly influenced by the experiences gained from the conflagrations of the last century.[1]

Since Greek antiquity and the works of Hippocrates (460 - 370 BC) amputation of the lower limb has been the surgical method of choice to treat open fractures and major lower limb trauma. Amputation methods have been refined over many centuries incorporating concepts such as proper wound cleansing, hemostatic ligation, debridement of necrotic tissues, and creation of a prosthetic-friendly stump.[2–4]

The 19th century marked major developments in the development of surgery in general and lower limb traumatology in particular with the discovery of anaesthesia, antisepsis and microbiology and hence the concept of infection. However, until the 20th century amputation remained the only surgical method of treatment for severe lower limb trauma.

The 20th century, with the 2 world wars and multiple other major conflagrations, produced a nefarious development of ballistics and as a result generated trauma with previously unimaginable tissue destruction, thus necessitating the development of plastic-reconstructive surgery which established and consolidated its essential role in the treatment of severe lower limb trauma. [1,6]

The many general surgical and medical developments of the modern period have led among other things to the definition and characterisation of the following key concepts in lower limb reconstruction: amputation versus reconstruction; ideal timing of treatment; bone stabilisation; vascular reconstruction; peripheral nerve reconstruction; bone reconstruction; soft tissue reconstruction.

We will briefly describe the most important aspects of these concepts and then in the next chapter we will detail the evolution of flap reconstruction techniques in the lower limb.

- Amputation vs. reconstruction

In the treatment of the patient with complex lower limb trauma it is important to understand that unsuccessful attempts to preserve the extremity have major physical, mental, social and financial implications. Despite major advances in microsurgical reconstruction, bone regeneration or infection therapy in recent decades many patients undergo a series of reconstructive surgeries only to end up with limb amputation. It is therefore important to try to identify these patients at an early stage in order to offer each patient the option that maximises function and rehabilitation potential.

A number of factors may contribute to predicting the need for amputation such as:

- Gustillo IIIC tibial fractures
- Ischial or tibial nerve injury
- Prolonged ischaemia (> 4 - 6 hours) or muscle necrosis
- Major soft tissue decussation or contusion
- Severe wound contamination
- Multiple/severe comminuted fractures; bone defects
- Advanced age or severe co-morbidities
- Failed revascularization / prediction of failed revascularization

- Ideal timing of treatment

One of the few certainties in the treatment of open lower extremity trauma is that these patients should be treated initially by generous debridement of devitalized tissues and extensive irrigation of open fractures. It is generally considered standard practice for patients with open fractures to arrive in the operating room within 6 hours of trauma. However, this temporal desideratum is not supported by clear evidence. [8]

Regarding the ideal timing of reconstruction most experts support the idea that early reconstruction leads to better outcomes. The most cited study in this field is that of Marko Godina[9] in 1986 who analysed the timing of microsurgical reconstruction in 3 groups according to the duration since the initial trauma:

1. Immediate reconstruction: within the first 72 hours
2. Delayed reconstruction: between 72 hours and 3 months
3. Secondary reconstruction: after 3 months

The study clearly shows that optimal results are obtained in the immediate reconstruction group followed by the delayed and secondary reconstruction groups.

However, it is important to recognise that immediate reconstruction is not a feasible option for every patient, for example due to the presence of other severe injuries requiring emergency treatment or due to the lack of institutional and personnel infrastructure to be able to provide debridement and reconstruction in one emergency procedure.[14]

If these conditions cannot be provided, repeated debridement and the deployment of a continuous negative pressure dressing (e.g. VAC system, KCI Medical Systems) prior to definitive reconstruction may be the optimal strategy.

- Bone fixation / fracture treatment

The initial orthopaedic management of an open lower extremity fracture is traditionally based on the use of external fixator in an effort to avoid implantation of osteosynthesis materials in a possibly contaminated operative field. Recently more and more traumatologists are choosing to fix open fractures immediately using intramedullary rods or even plates and screws using a technique called minimally invasive osteosynthesis[14].

- Vascular reconstruction

Although complete vascular lesions are rare in lower extremity trauma, patients often present with clinical signs suggestive of compromised vasculature. However, these are often caused by haemorrhage from soft tissue injuries or fractures, traction of otherwise intact arteries with consequent loss of pulse or compartment syndrome. However it is prudent that actual vascular lesions be excluded, so the use of appropriate imaging methods is recommended.

Prompt therapy of any severe vascular injury in lower limb trauma is obviously an absolute surgical indication, the duration of ischaemia ultimately determining the chances of tissue survival, especially muscle tissue.

Also, the operative sequence in combined bone and vascular injuries is often debated. Thus there is on the one hand the concept of immediate vascular treatment to reduce the duration of ischaemia and on the other hand there are authors who favour initial bone stabilisation to avoid possible iatrogenic injury of vascular reconstruction during fracture treatment. A meta-analysis comparing the results of the two concepts of operative sequence showed no clear difference between the two groups in the rate of secondary amputation.[20]

- Peripheral nerve reconstruction

Until the late 19th century suturing and nerve reconstruction were generally not practiced due to unsatisfactory results. It was not until 1873 and 1917 that epineural and fascicular neurorrhaphy were described for the first time. Also at the end of the 19th century the first truncal nerve graft was reported and in 1939 Bunnell and Boyes introduced the cable graft, but it would take until 1972 for Millesi, based on Sunderland's extensive studies of nerve topography, to describe interfascicular topographic nerve grafts[21]. The results of nerve reconstruction in the lower limb remain inconsistent and depend significantly on surgically immutable factors[22].

- Bone reconstruction

Options for bone reconstruction in the lower extremity include autologous bone grafting, vascularized bone transfer, and distraction osteogenesis, including the Ilizarov technique.[24] Autologous bone grafts are used for small defects. The most commonly used vascularised bone flap is the free fibular flap[25], and as alternatives the vascularised iliac crest and scapular bone flap or osteocutaneous flap. For defects exceeding 10 cm distraction osteogenesis may be a treatment option.

- Soft tissue reconstruction

For the ideal management of the patient with a severe traumatic lower limb injury it is important to consider a wide range of options for soft tissue reconstruction, choosing the one that is safest and can lead to the best functional outcome.

Generally, it is useful to distinguish the flaps used in the lower limb into local, pedicled and loose flaps.

Local flaps are a viable option in the reconstruction of lower limb defects as long as their vascularity has not been affected by the initial trauma. The advantages of local flaps are the operative time and the reduced complexity of the procedure[26]. Local flaps also use tissues similar to those to be reconstructed. Traditionally muscle flaps are a good option in upper and middle thigh reconstruction.

The alternative to local flaps is microsurgical free flaps, which many authors consider to be the first reconstructive indication in the lower limb and especially the calf. For microsurgical transfer in lower limb reconstruction, free muscle flaps on the one hand and fasciocutaneous flaps on the other are suitable.

Muscle free flaps allow the obliteration of virtual gaps and are a robust option for covering even large defects[27]. The alternative to free muscle flaps is fascio-cutaneous flaps which have the advantage that they can be easily re-lifted for secondary surgery.

2.2 Evolution of flap reconstruction techniques in the lower limb

In general the history of flap reconstruction in the lower limb has developed in parallel with the history of flaps in general, a particular aspect in the lower limb being the recognised difficulty in reconstructing this region and in particular the calf.

Although evidence of the first cutaneous flap can be found in the writings of Sushruta as early as 600 BC, progress in tissue flap surgery has been held back for millennia due to the absence of knowledge of tissue vascularisation and in particular the tegument, and the lack of cultural exchange between different parts of the world[32,33].

In the 19th century, however, anatomical knowledge of skin vascularisation was dramatically changed by the work of Carl Manchot[35] and Michel Salmon[36], and in parallel with this knowledge, new techniques of flap reconstruction were developed that would become the basic surgical procedures in lower limb reconstruction.

With the 20th century and the increased need for reconstruction due to multiple and severe trauma resulting from the wars of this century reconstructive surgery developed significantly. It is perhaps interesting to note that among the earliest uses of the distal flap was Hamilton's 1854 description of the "cross leg" flap[37]. Distal flaps or pre-conditioned flaps have long been the standard in lower limb reconstruction.

McGregor and Jackson[41] explored the importance of the axial vascularisation of the flaps, describing for the first time the inguinal flap. This flap was to become famous with the development of reconstructive microsurgery in the 1970s.

Once the microsurgical anastomosis barrier was overcome, the development of free flap transfers to the lower limb accelerated, with the first free flaps described being the iliac crest and fibula free bone flaps, also for lower limb reconstruction, in this case of bone defects[25]. The 1980s brought with it the description and development of microsurgical free transfer of muscle and musculocutaneous flaps. Marko Godina and Andrej Banic first developed and described free transfer of the latissimus dorsi muscle for lower limb reconstruction, and this and other muscle flaps became the main method of reconstruction of posttraumatic defects of the lower leg[45,46].

Despite the popularity of muscle flaps, their disadvantages such as the possibility of functional disorders of the donor site have led some surgeons to explore new possibilities. Thus Ponté famously reintroduced another option of local flaps to the lower limb, using fasciocutaneous flaps which offered an excellent survival rate and were nicknamed "superflaps" by the author[47].

After all, as Ponté's flaps were later shown to be vascularised by lower limb fasciocutaneous perforators, it was only a matter of time before the use of these perforators would revolutionise reconstructive surgery, particularly in the lower limb. Particularly important in the development of perforator-based flaps is the work of Taylor and Palmer who described the concept of angiosteam[48]. In 1989 Koshima and Soeda[49] described the first perforator-based flap (in the lower abdomen). This was followed by the description of the anterolateral thigh flap (ALT) introduced by Song[51] and popularised especially in the lower limb as a free flap by Fu-Chan Wei, who considered it an "ideal flap"[52]. Further development of lower limb reconstruction is characterised by local perforator-based flaps with the next important step being the "propeller" flap, first described by Hyakusoku[53], developed by Hallock and Teo[54,55] and widely applied to the upper and lower limb by Georgescu in Cluj in Romania[56].

2.3 Perforator-based flaps in the lower limb

The lower extremity is an anatomical region rich in vascular perforators that may represent the pedicle of local flaps. These perforators have been extensively studied and detailed by anatomical and angiographic research[58-60].

The source arteries of perforator-based flaps in the thigh are :

1. Superficial femoral artery with direct perforators at the medial thigh region.
2. Superficial iliac circumflex artery with perforator branches at the inguinal region.
3. Lateral circumflex femoral artery with perforators mainly in the anterolateral tegument of the thigh.
4. Medial circumflex femoral artery providing vascularization of the posteromedial thigh.
5. The deep femoral artery provides through its perforating branches the vascularization of the posterior thigh.
6. Medial and lateral superior geniculate arteries providing vascularization to the distal thigh.

In the knee region, flaps can be raised based on musculocutaneous perforators originating from the femoral artery as well as based on multiple septo-cutaneous perforators originating from the descending genicular artery, the medial superior and lateral superior genicular arteries and the medial inferior and lateral inferior genicular arteries[61]. The vascularization of the integument in the knee area also involves the recurrent anterior tibial artery and the popliteal artery with direct cutaneous branches. The saphenous artery is a superficial branch of the descending geniculate artery and is the base of the saphenous perforating lamina which may incorporate the eponymous nerve thus creating an innervated flap. In the popliteal region the medial and lateral sural arteries are direct branches of the popliteal artery and may be the source of perforator flaps e.g. medial sural artery perforator flap (MSAP).

In the lower leg, perforator flaps may be based on perforators originating from the posterior tibial artery, anterior tibial artery and fibular artery[61]. Perforators originating from the posterior tibial artery are found in the intermuscular septum between the soleus muscle and the flexor digitorum longus muscle. Anterior tibial artery perforators are either musculocutaneous at the level of the tibialis anterior muscle or septocutaneous between the tibialis anterior muscle and the extensor hallucis longus muscle. Also, a series of perforators in the anterior tibial artery can be found in the anteromedial septum between the extensor muscle compartment and the peroneus brevis muscle. Perforators based on the peroneal artery are mainly found in the postero-lateral septum between the peroneus longus muscle and the soleus muscle.

In the foot the terminal branches of the anterior tibial, posterior tibial and fibular arteries are the sources of the calcaneal and medial plantar perforator flaps.

2.3.1 Vascular anatomy of the integument of the leg

The knee and leg region accounts for 34% of the total integumentary surface of the lower extremity (7% of the total body surface area). The integument of this region is vascularised by approximately 30 ± 13 perforators with a diameter of 0.7 ± 0.2 mm. A perforating pedicle vascularises on average a tegumentary area of about 40 cm². Five vascular territories can be distinguished in the calf with the following source arteries:

- descending genicular artery
- popliteal artery
- posterior tibial artery
- anterior tibial artery
- fibular artery

2.3.2 Pedicled perforator-based flaps based in the lower leg

Perforator-based flaps in the lower leg represent a turning point in the continuing evolution of reconstructive techniques to reduce surgical morbidity. The development of the propeller flap concept was an important step forward for the application of perforator-based reconstructive techniques in the distal calf, a region known for its difficulty in soft tissue reconstruction. Hyakusoku et al[53] first used the term propeller flap (LP) to describe an insular flap attached by a wide central pedicle containing no identified vessels. This pedicle restricts the maximum possible rotation of the flap to 90°, thus limiting the applications of this technique. In contrast, the modern propeller flap, introduced by Hallock[54] and perfected by Teo and Georgescu[55,56,67,68] is based on a single perforator thus making it possible to rotate the flap up to 180° around the perforating axis, thus significantly broadening the possibilities of this reconstructive technique.

The propeller flap concept

The propeller lamellar is, simply defined, a locally fascio-cutaneous insularized lamellar based on an extensively dissected perforator fuse. The LP is designed with this perforator representing the pivot around which the 2 ends of the flap, of different lengths, can be rotated so that the longer end can easily cover the tissue defect. The possibility of rotating this flap up to a maximum of 180° makes it extremely versatile, making it a good option for reconstructing traumatic defects of the distal calf region (Figure 4).

Surgical indications

Although the propeller flap can be used to cover defects in the middle and upper third of the calf or the knee region, its major utility lies in the possibility of reconstructing defects in the distal third of the calf. These defects often result either directly as a result of trauma, may result from postoperative complications after osteosynthesis of malleolar fractures, repair of Achilles tendon ruptures or tibiotalar arthroplasty, or may result from tumour resections, decubitus ulcers or chronic venous ulcers.

Surgical technique considerations

The correct use of an LP requires a flexible attitude in the design and erection of the blade. The following considerations are important for the correct application of the LP technique.

- Location, type and size of the defect.
- The course of the source artery and the location of the perforators.
- Potential length and dimensions of the flap.
- Determination of the amount of healthy tissue adjacent to the defect.
- Avoidance of donor site morbidity.

Importance of the propeller flap technique in the lower leg

The ability to use a flap based on a single perforating pedicle located close to the defect gives the reconstructive surgeon unparalleled freedom in the design of local flaps. Thus the propeller flap is an extremely versatile method in the calf where there is very little tegmental laxity, especially in the distal area55. This surgical technique opens multiple avenues to allow coverage of the notoriously difficult distal calf area quickly and safely even in units with limited reconstructive microsurgery resources. Although this surgical technique is very promising, with increasing experience in its use some detriments are highlighted so that its application must be subject to a lucid and fair analysis based on consistent experimental and clinical studies taking into account also the possible undesirable effects and outcomes of the technique.

2.4. Current problems of pedicled perforator flaps in the lower leg

The discovery and development of perforator-based flaps proved to be a major step towards minimizing donor site morbidity. By demonstrating the clinical reliability of microsurgical dissection of perforating vessels, it has become possible to harvest the tissue needed for reconstruction without sacrificing functionally important muscle, fascia, vascular and neural elements. Particularly in the case of perforator-based local flaps, this method allows reduction of the complexity and duration of reconstructive surgery with limitation of morbidity to the area of the defect itself and harvesting of tissue similar to the deficient tissue using tissue adjacent to the defect. Although to date there has been extensive clinical research on perforator flaps and many types of perforator flaps have been established as standard methods in some reconstructive approaches, the main problem with these flaps is the inability to accurately determine the volume of tissue that can be maximally harvested based on a single perforator. Thus, the known and feared problem of classical axial and randomized flaps, namely partial necrosis, has transferred to perforator flaps, but the methods to avoid this complication need to be rethought and a new paradigm of perforator flaps needs to be constructed based on experimental research results.

In recent years, many researchers have focused on pharmacological methods to reduce the rate of flap necrosis[72,73], and although promising data have been obtained experimentally, the transition of these results into clinical practice has not been possible. On the other hand, numerous anatomical studies related to perforating vessels have shown that anatomical variations in these cases are the rule rather than the exception, so the development of techniques to actively influence the volume and thus the maximum viable surface area of perforator-based flaps regardless of the given dimensions of the perforating vessel is of great interest.

Although it would seem obvious that perfusion in perforating vessels is the main determinant of the viable area of the flap, very little experimental research has been undertaken in this area and virtually no method of actively increasing blood flow in a perforator has been experimentally evaluated. In addition, although clinical experience shows that flap necrosis on perforators is usually due to venous rather than arterial insufficiency, there is very little experimental data assessing venous flow in these flaps. There is thus a niche in experimental research of flaps on perforators that we will try to explore in the experimental part of our study.

Clinical research into flaps on perforators is certainly attractive and many centres internationally have adhered to this method, the indication of which is continuously expanding in many areas of reconstructive surgery. Of course, with the sometimes forced expansion of the indications of a surgical method, the rate of failure and complications is likely to increase. Particularly with regard to the reconstruction of lower limb defects, standard methods (free flaps) have been partially or even exclusively replaced in some clinics by perforator-based local flaps. The unit where the author works presents an ideal situation related to the possibility of a detailed and complete analysis of cases of reconstruction with propeller flaps, on the one hand due to the extensive traumatic caseload and on the other hand due to the relatively recent (since 2014) use of the LP technique, all operations using this technique being performed by the PhD student. Thus, cases can be followed prospectively which results in high quality data without risking the loss of information inevitable in a retrospective study.

2.5. Research objectives

As detailed above we are feel that perforator-based flap research should be complemented by experimental and clinical data that on the one hand determine the ideal way to actively influence flap survival through direct manipulation of arterial or venous blood flow to the pedicle itself and to provide comprehensive, prospectively collected clinical data on the results of the propeller perforator flap technique for the reconstruction of post-traumatic lower limb defects, and here in particular of the calf where the potential but also the greatest risks of the LP lie. We will further describe the objectives of our research approach and in the practical part we will detail the actual studies and their results.

2.5.1. Experimental study

The objective of the experimental study is to analyze the influences exerted by increasing arterial flow and/or reducing venous return pressure at perforating vessels in an experimental model on the viability rate of a perforator-based flap. The innovation of this experimental approach is to actively modify blood flow parameters in perforating vessels rather than relying on anatomical characteristics of these vessels to achieve a viability advantage.

2.5.2. Clinical study

The objective of the clinical study is to analyse in detail the indications and clinical outcomes of lower limb defect reconstructions performed with perforator-based local flaps in a prospective, single-centre study with the same operator performing the reconstructive procedures.

3. PRACTICAL PART

3.1 Experimental study

3.1.1 Preliminary considerations

Advances in knowledge of perforator vessel anatomy and skin perfusion physiology have allowed clinicians to use the perforator-based flap technique in the reconstruction of various soft tissue defects[74,75]. The pioneers of this technique, Koshima et al. marked the beginning of the perforator-based flap era in 1989 with the publication of the first flap based on the inferior epigastric artery without the inclusion of the rectus abdominis, this technique having a major impact in reducing donor site-associated morbidity[49]. Subsequently, many researchers and clinicians have worked hard to expand the areas of use of this new surgical technique, with one of the important steps being the development of pedicled perforator-based flaps[76] that do not require microsurgical anastomoses. Although perforator-based pedicled flaps clearly have multiple surgical advantages such as reducing donor site morbidity and surgical duration[77], some authors have reported an increased rate of partial necrosis of this type of flap[78,79]. For this reason many researchers and surgeons have sought methods to improve the survival of perforator-based flaps.

Vascular flow modifications, either with the aim of increasing arterial flow or optimising venous drainage, have been frequently used by researchers to improve the survival rate of perforator-based flaps. However, the results of this research have been largely inconclusive[80-84]. It is also important to note that these methods of altering blood flow in perforator-based flaps rely exclusively on the addition of additional arterial or venous sources in the form of additional pedicles. However, this method is difficult if not impossible to apply in the clinic where additional pedicles severely limit the degree of rotation and thus the main reconstructive advantage of perforator-based local flaps.

Based on the above considerations we designed our experimental study with the aim to evaluate the effects of optimizing the arterial and venous flow in the pedicle proper of the flap on its survival, choosing as experimental model a flap based on musculocutaneous perforators in the rat.

3.1.2 Material and methods

A total of 35 Lewis rats with an initial weight between 250-300 g were used for this study. All animals were treated in accordance with the legal requirements for animal experiments (Public Health Service Policy in Humane Care and Use of Laboratory Animals) throughout the experiment. Rats were fed standard laboratory chow and unrestricted water consumption throughout the observation period and their health status was monitored daily. This study was approved by the Ethics Committee for Animal Experiments of the Canton of Bern, Switzerland (approval number 89/16).

Based on the model described by Coskunfirat et al[85], a flap based on the posterior musculocutaneous perforator of the thigh was elevated in all animals and the musculocutaneous perforator was dissected until its emergence from the femoral vessels. Animals were randomly assigned to the following experimental groups according to vascular pedicle changes as follows:

I. Control (n=10): no pedicle changes, lambus re-sutured in original position.

II. Immediate arterial optimization (n=10): a ligature is placed on the femoral artery distal to the emergence of the perforating pedicle at the time of flap elevation, then the flap is re-sutured in the original position.

III. Arterial pre-optimization (n=5): Through an inguinal incision the femoral artery is ligated distal to the emergence of the perforator pedicle 5 days before the flap is lifted. The flap elevation procedure is identical to group I (control).

IV. Venous pre-optimization (n=5): Through an inguinal incision, ligation of the femoral vein distal to the emergence of the perforating pedicle is performed 5 days before the flap is lifted. The flap elevation procedure is identical to group I (control).

V. Venous pre-optimization and immediate arterial optimization (n=5): Through an inguinal incision the femoral vein is ligated distal to the emergence of the perforating pedicle 5 days before the flap is lifted. At the time of flap elevation, a ligature is placed on the femoral artery distal to the emergence of the perforating pedicle, then the flap is re-sutured in the original position.

All procedures were performed under continuous inhalational anesthesia. Isoflurane 5% with oxygen (1 L/min) was used for induction of anesthesia (2-3 min) in an induction chamber. Rats were then placed under maintenance anesthesia with Izoflurane 1-1.5% and 0.6 L/min oxygen. All rats were maintained in isothermia using thermal supports and treated with ophthalmic ointment to prevent conjunctival desiccation. All animals were treated with preemptive analgesia with Buprenorphine (50 μg/kg) subcutaneously at 30 min preoperatively and then postoperatively as needed (assessed using a standardized laboratory animal welfare checklist).

3.1.2.1 Surgical technique and flap raising

After removal of hair at the right posterior half all rats were marked as follows: a rectangular flap 9 cm long and 3 cm wide was drawn from a line joining the anterior knee joint and the posterior ischial tuberosity. The central axial line of the rectangle was drawn and the following points (P1-3) were marked on it as follows (Figure 5):

- P1 - 2 cm cranial from the caudal limit of the lambium (approximately at the level of the perforator).
- P2 - 3 cm cranial of P1
- P3 - 3 cm cranial of P2

After incision of the entire flap, the flap was raised retrograde under the fleshy panniculus until the posterior thigh perforator, which perforates the biceps femoris muscle, was identified (Figure 6). The perforating pedicle was then carefully dissected, leaving a muscular cuff around the perforator so as not to injure it (Figure 7).

The perforator was followed until emergence from the femoral vessels at the medial level of the thigh. An additional incision was placed here in the inguinal crease to provide access to the femoral vessels (Figure 8).

After making changes to the femoral vessels according to the previously detailed group division (Figure 9) the flap was sutured in place with a continuous intradermal 5-0 PDS thread suture (Figure 10). In the pre-optimization groups (groups II and III) a groin incision was made 5 days before flap elevation to perform the vascular changes described.

Immediately before skin suturing, analgesia was applied with subcutaneous Buprenorphine (50 g/kg). The same analgesia was administered every 12 hours until the second postoperative day or when the animals showed clinical signs of pain (according to the standardized laboratory animal welfare checklist).

Rats were monitored 7 days postoperatively and daily health assessments were performed based on the approved standardized laboratory animal welfare checklist. All rats were euthanized on postoperative day 7 by injecting 150 μg/kg pentobarbital intraperitoneally, and death was confirmed by bilateral thoracotomies.

3.1.2.2 Flap assessment

3.1.2.2.1 Digital planimetry

$$\text{Flap viability} = \frac{\textit{viable area (number of pixels)}}{\textit{total area (number of pixels)}}\ x\ 100$$

3.1.2.2.2 Laser-Doppler assessment

Laser Doppler flowmetry was performed with the Aïmago® EasyLDI flowmetry camera (Aïmago SA, Lausanne - Figure 11) at all marked points (P1, P2, P3) before the slide lift, after the slide lift, immediately after completion of the operation and then at POD 1 and POD

3.1.2.2.3 Statistical analysis

Data analysis was performed with SPSS v21.0 (IBM Corp., Armonk, NY, USA). Kruskal-Wallis non-parametric test was used to compare fluxmetry between the 3 groups. Subsequently, pairwise comparisons were performed using Dunn's procedure with a Bonferroni correction for multiple comparisons. A one-way ANOVA and Tukey-Kramer post-hoc analysis were used for normally distributed digital planimetric measurements. Results were considered statistically significant for $p < 0.05$.

3.1.3 Results

3.1.3.1 Digital planimetry

All flaps showed an area of typical distal necrosis (Figure 12). The survival area of the flaps was statistically significantly different between groups, $F (4.29) = 18.82$, $p < 0.001$. Figure 13 shows the graphical representation of the digital planimetry results. Data are presented as means ± standard deviation. The highest survival area was found in group II (78.12 ± 8.38%), followed by group V (74.33 ± 8.21%), group III (71.85 ± 1.76%) and group IV (60.35 ± 2.41%). The control group (I) had the lowest values: 56.55 ± 8.38%.

3.1.3.2 Laser – Doppler

Blood flow distributions were similar for all groups in all tests as assessed by visual inspection of the boxplots.

3.1.3.2.1 Results for P2

Figure 14 shows the median percentage values obtained in P2 for all groups. The only statistically significant difference between groups was observed in POD 7 where group II had higher values than group I and IV ($p = 0.026$ and $p = 0.039$ respectively).

Within-group analysis revealed a statistically significant decrease in flux between measurements taken before lamella lift and POD 1 ($p < 0.05$) in all groups. Flow improvement was statistically significant between POD 1 and POD 7 in all groups ($p<0.05$), except group III (pre-arterial lift). Group II (immediate arterial optimization) showed a significant increase in flow from a median value of 85.49% preoperatively to 135.8% on POD 7.

3.1.3.2.2 Results for P3

As illustrated in Figure 15, there was a decrease in flux in all groups between measurements taken after the blade lift and POD 7 ($p < 0.05$). The difference between flow before blade lift or before vessel manipulation and POD 7 was statistically significant in all groups ($p<0.05$) except group II.

At POD 7, group II was the only group to show an increase in flow compared to POD 1 ($p<0.05$), while all other groups continued to have lower values compared to previous measurements.

3.1.4 Discussion

The innovation of our experimental design lies in a different way of manipulating vascular flow within the pedicle proper of the flap by ligating the femoral artery distal to the perforator, thus directing all femoral artery flow to the flap.

This novel approach does not require the addition of an additional vascular pedicle, as has been done by other researchers investigating arterial augmentation of flap. This solution is derived from clinical experience with flaps on pedicled perforators and in particular 'propeller' flaps, where, due to the need for flap transposition, an additional vascular pedicle may make the procedure impossible.

Our digital planimetry results clearly show that optimizing arterial inflow and not optimizing venous drainage in the flap pedicle leads to increased flap viability. Our data also suggest that it makes no difference whether arterial flow optimization is performed acutely or as a preconditioning strategy.

Our study clearly shows that flow optimization at the pedicle of the flap has significant effects on flap survival in a rat muscle-cutaneous perforator flap model. Although Laser Doppler data suggest involvement of the complex vessel-vent system, the mechanism underlying these changes remains largely unknown. Nevertheless, we believe that the promising results of this study warrant a detailed examination of the mechanisms involved in the beneficial effect on the observed flap viability rate.

3.1.5 Conclusions

Optimization of arterial flow in the pedicle of a rat musculocutaneous perforator leads to increased flap survival whether performed acutely or as a preconditioning strategy, whereas optimization of venous flow has no effect on flap viability. These results could have clinical implications, but more precise characterization of the mechanisms involved in the effects on flap viability observed in our study is first needed.

3.2 Clinical study

3.2.1 Preliminary considerations

Tissue and soft tissue defects of the lower leg and foot continue to be a challenge in reconstructive surgery. The laxity of the integument in this region and the amount of subcutaneous tissue are reduced and the oedema and tension resulting even from primary surgical suturing of small defects often leads to wound healing complications. From the point of view of reconstructive surgery microsurgical free flaps have crystallized as the first surgical option in the coverage of lower leg[95,96] and foot defects but the complexity and duration of the operation together with the known failure rate of these procedures do not allow the technique to be used in every patient and in every plastic surgery unit. The alternative of random-pattern pedicled local flaps is virtually useless in the calf due to the limited maximum size of these flaps and the need for a very wide-based pedicle tegument[97]. In these circumstances, perforator-based local flaps, especially the "propeller" type developed in recent years, offer an extremely valuable alternative in calf and leg reconstruction due to their main advantages: reduced operative time and secondary morbidity.[76,78,98]

Although initially considered a true revolution for lower limb reconstruction, with the accumulation of clinical experience it has become clear that in the lower limb the postoperative complication rate of propeller flaps is relevant. The influence of this complication rate on the reconstructive outcome, i.e. the causal link between postoperative complications and eventual reconstructive failure, is however still uncertain. Also uncertain for the moment are the causes for postoperative complications.

Our study aims to analyse the experience of the Plastic Surgery Clinic of the University Hospital Bern - Inselspital with this reconstructive technique prospectively in consecutive patients in an attempt to find causal relationships between the characteristics of the patients and the operative procedures and the occurrence and effects of postoperative complications.

3.2.2 Material and methods

All patients who underwent propeller flap reconstruction of the lower limb distal to the knee joint between 2014 and 2017 were enrolled in this study. Demographic, operative and postoperative follow-up data were collected.

Surgical data including flap size, perforator details, donor site closure modality, duration of surgery and source artery of perforator is presented in Table 3.

3.2.2.1 Surgical technique

3.2.2.1.1 Preoperative marking

The relevant perforators were marked intraoperatively at the lateral aspect (for fibular artery) or medial aspect (for posterior tibial artery) of the patient's calf. Specifically, for defects at the lateral aspect of the calf, the line joining the head of the fibula to the point of maximum prominence of the lateral malleolus was initially drawn. A dotted line was drawn approx. 2.5 cm posterior to this, this line representing the cutaneous projection of the postero-lateral calf septum. Following this line with the vascular Doppler, perforators originating from the fibular artery were marked. In the case of a defect in the medial aspect of the calf, a similar procedure was used to detect perforators in the antero-medial septum along a line parallel to the medial border of the tibia and located 1.5 cm posterior to it (Figures 16 and 17).

3.2.2.1.2 Surgical technique

The patient is positioned in dorsal or lateral decubitus depending on the location of the defect and the planned flap. A tourniquet was used without complete exsanguination of the lower limb to allow better visualization of the perforators. After surgical treatment of the defect (tumour resection, debridement of posttraumatic, postinfectious wounds or chronic ulcers) it was measured and the planned flap was drawn with the pedicle based on the perforator closest to the integumentary defect (Figure 18). Initially only one side of the planned flap (in the vast majority of cases the anterior edge) was incised up to and including the deep fascia and dissection continued subfascially from distal to proximal and anterior to posterior until the perforators were identified and dissected to emergence from the source arteries and veins (Figure 19).

Separation of the perforating artery from the comitant veins was not performed but rigorous attention was given to separating the perforating pedicle from any septal and fascia flanges that could lead to compression of the vessels following rotation (pedicle skeletonization). The tourniquet was then deflated and the final choice of perforator was made based on the presence of visible pulsations or the highest intensity Doppler signal. After choosing the perforator as the pedicle, the flap design was adjusted if still needed and then the entire flap was incised and released subfascially completely except for the perforating pedicle (Figure 20). Depending on the location of the defect the flap was rotated with the minimum arc of rotation required to achieve complete coverage of the defect (Figure 21). Suturing and application of passive or active drainage was performed as needed. The donor area was either primary sutured or covered with split loose skin grafts (Figure 22). A plaster splint was applied to the operated calf, with particular care to avoid compression of the splint at the level of the flap.

3.2.2.1.3 Postoperative follow-up

In the first 48h postoperatively the lambus was monitored at 2h intervals in the first 24h and then at 4h intervals in the next 24h controlling colour, turgor, tegumentary temperature and Doppler signal at the pedicle level. After 5 days postoperatively, decubitus positioning of the lower limb was allowed for daily incremental intervals. Elastic compression of the operated limb was allowed after postoperative day 10 and walking with support on the affected limb was allowed (in the absence of other contraindications) after 2 weeks after surgery. In general, healing of the flap is complete after 2 weeks if no postoperative complications have occurred (Figure 23).

3.2.2.2 Statistical analysis

Statistical analysis of the data was carried out with SPSS software. Fisher's exact test for independence was used to analyze categorical variables. Point-biserial correlation coefficient was used to analyze the relationship between complications and age, defect area, lambar area and lambar rotation arc. The Mann-Whitney test was used to compare the duration of hospitalization and time to complete healing between patients with and without postoperative complications, respectively. A p-value < 0.05 was considered statistically significant.

3.2.3 Results

A total of 26 patients met the eligibility requirements. Eleven patients were male and 15 female. The patients' ages ranged from 17-91 years (mean 60 years). None of the patients were lost to postoperative follow-up before definitive wound healing. Postoperative complications and details, as well as length of hospitalization and time to definitive healing are shown in Table 3. Of the 9 patients (34.6%) who experienced postoperative complications only 3 (11.5%) required reoperation. One patient with minimal partial lambial necrosis had a wound infection requiring further debridement and a small bipedicle local flap for definitive coverage, a patient with extensive partial lambar necrosis subsequently required a microsurgical free flap for defect coverage and a third patient with complete lambar necrosis was treated by wound conditioning with a VAC system and then definitive defect coverage with a dermal substitute (Matriderm , MedSkin Solutions Dr. Suwelack AG, Germany) and split free skin graft. All other complications were treated conservatively with dressings and repeated consultations. Duration to complete healing ranged from 2 to 32 weeks with a mean of 6.3 weeks.

There was a statistically significant association between complications and polymorbidity and between complications and the source artery of the flap. The presence of polymorbidity was strongly correlated with the occurrence of postoperative complications ($p<0.0001$) and peroneal artery-based LPs were also correlated with postoperative complications ($p=0.015$).

A statistically significant difference was identified between the number of weeks to complete healing and length of hospitalization when comparing patients with postoperative complications versus those without complications. Thus, patients with postoperative complications required more days of hospitalization ($p=0.03$) and more weeks to complete healing ($p<0.001$).

3.2.4 Discussion

According to the Ghent consensus, perforator flaps are subcutaneous tissue and integumentary areas vascularised by perforating arterial and venous branches originating from a deep vascular axis. These vessels can either penetrate muscle tissue (musculocutaneous perforators) or circulate at the level of intermuscular septa (septocutaneous perforators).74 The development of this technique has been facilitated by extensive studies of lower limb vascularization and a better understanding of the principles of flap vascularization.[99-101]

Although free flaps are considered the standard method in lower limb reconstruction, propeller flaps have become increasingly popular today.[9,77,95,102 -104] The texture and colour of the tegument is closer to that of the reconstructed area, the suppleness of the tegument is a real advantage and the operative time is significantly reduced compared to free flaps (Figure 24).[97,98,105-107] Moreover, some studies show that the complication rate between microsurgical free flap reconstruction and local perforator-based flaps does not differ significantly.[77,78]

However, there are also disadvantages to using LP in lower limb reconstruction. Probably the most important is the proximity of the donor site to the trauma site with the risk that the vascularity of the flap may be impaired. Furthermore, dissection of the lambus may lead to injury to superficial sensory veins and nerves with increased risk of oedema and postoperative pain.[74]

Of particular note is the discussion of reconstruction of the distal third of the calf in patients with associated diseases. In this group of patients the increased complication rate in both classic local flap and free flap reconstruction is well known. In these circumstances the LP technique represented the hope of improving outcomes. Indeed, some studies show that LP based on ATP or AP perforators can also be used successfully in patients with relevant associated pathology.[110,111]

In our study, all 9 patients with associated pathology meeting the definition of polymorbidity experienced postoperative complications, but interestingly, only 1 patient required surgical reintervention (Figures 25 and 26). In contrast, only 2 of the 18 patients without significant associated pathology experienced postoperative complications, but both patients required reoperation (Figures 27 and 28).

Diabetes[79,115], ACOMI and age over 60 years have been identified in the literature as risk factors for LP failure.[79] In our study, no statistically significant age-related difference could be determined between the groups with and without postoperative complications.

As described by other authors, the PTA perforator-based LP is the safest lower limb flap of its type76 and our results support this claim, given that only one of the patients treated with PTA LP suffered postoperative complications. in the case of PA LP, complications were found in 8 of 11 cases. However, these results should be interpreted with caution, as in most cases the choice of arterial source of LP is predefined by the location of the defect and is not an independent variable. Our study suggests that in lateral calf defects, the indication for LP reconstruction should be carefully considered, whereas ATP-based LPs are a significantly more reliable solution if they can be applied.

Although there thus seems to be a partial consensus on risk factors in lower limb LP reconstruction, it should be noted that some authors have not identified specific risk factors for postoperative complications[98]. Thus, the use of LP in patients with significant associated pathology (e.g. ACOMI) is still supported by some authors, mainly due to the reduced operative time and minimal donor site morbidity.[116] These authors accept the increased risk of minor postoperative complications with rigorous patient selection.[105]

Also in our study the complication rate was high in polymorbid patients, but most complications were minor, without the need for reoperation. Only one flap was lost in this group, all other patients achieved secondary local healing. Length of hospital stay did not differ statistically significantly between the group with postoperative complications and the group without. The only statistically significant difference was observed in the duration to complete healing, on average 2 weeks if no complications occurred, but between 4 and 36 weeks in the group with postoperative complications.

One of the limitations of this study is the relatively small number of patients. It could be explained by the restrictive indication of LP, free flap reconstruction being the method of choice in these cases in our clinic.

4. CONCLUSIONS, IMPORTANCE OF THE WORK AND FUTURE PERSPECTIVES

The subject of this work, perforator-based flaps in the treatment of soft tissue defects of the lower limb, is a highly actual issue in the context of modern plastic and reconstructive surgery.

As we have shown in the theoretical part of the paper, lower limb reconstruction has always been a topic of high relevance in the history of plastic and reconstructive surgery and in traumatology. Reconstructive microsurgery has been a major step forward in the attempt to save the lower limbs of patients, who on the one hand have been increasingly confronted with severe trauma related to the refinement of ballistic methods in wars but also related to the significant increase in high-speed accidents with major soft tissue damage and on the other hand have benefited from general medical developments that have allowed them to survive even extremely severe trauma. Thus, reconstruction of the lower limb is no longer a rarity in severe injuries, on the contrary, the desire of any reconstructive surgeon is to offer the possibility of saving the lower limb in almost any situation. Furthermore, the refinement of methods and the increase in the number of patients benefiting from lower limb reconstruction has led to intense research and attempts to improve functional and aesthetic outcomes. Saving the lower limb is no longer an end in itself but the goal of modern lower limb reconstructive surgery is found in the attempt to provide the maximum functional and aesthetic outcome with minimal associated morbidity.

Perforator-based flaps represent a very important step forward in achieving this goal as they allow harvesting of tissue perfectly adapted to the defect to be reconstructed without minimally affecting adjacent structures in the donor area. The development of these flaps has been made possible by detailed and extensive studies of the skin vasculature of the lower limb. Furthermore, local perforator-based flaps in the lower limb represent a further step forward by allowing the use of tissues adjacent to the defect that have virtually identical qualities to the lost tissue.

Between perforator-based flaps, in the lower limb and especially in the notoriously difficult to reconstruct area of the calf, propeller flaps represented a real revolution, allowing for the first time the safe use of large areas of local integument and soft tissue in a way that is ideal for the aesthetics of the donor area. As with any clinical development, however, with time and with the widespread uptake of the method in more and more centres, the limitations of this method became clear. Mainly the partial necrosis rate has been extensively and controversially discussed in clinical work. On the one hand some groups show impressive results with very few complications, including partial necrosis, while other groups have significantly increased complication rates.

Observatii

And in the field of basic research, a number of studies have started from this perceived high rate of partial necrosis trying to offer solutions, these mainly consisting of pharmaceutical interventions (virtually not used at all in the clinic) or the addition of vascular pedicles (venous and/or arterial) to flaps on perforators. Unfortunately, however, none of these studies has been able to formulate clear conclusions. Although it is clear that the addition of vascular pedicles (arterial supercharging / venous superdrainage) brings benefits in terms of flap survival, these interventions always involve a microsurgical step, which diminishes the advantages of these flaps.

For this reason we tried in the experimental study to change the strategy and modify the vascular flow IN the pedicle of the flap. We could clearly show that only arterial augmentation in the pedicle provides a survival benefit of the flap117. In short, regardless of the amount of arterial flow, the veins in the pedicle will be able to drain the lambus in any case. Our experimental study clearly shows important clinical considerations:

- Perforator preparation up to the level of the source vessel and its ligation distal to the perforator emergence is recommended in the case of a flap on locally pedicled perforators in all cases where this is clinically feasible.
- If the main source artery of a local pedicled perforator flap is already ligated or thrombosed distal to the perforator emergence a flap elevated to the first viable perforator proximal to the arterial thrombosis is safe (even safer than if the artery were in continuity) in terms of vascularity and is an ideal reconstructive option.

On the other hand, like any study, this one raises questions that are not fully answered. On the one hand, the experimental study is performed on a perforator-based flap model that is re-sutured in its original position without being rotated around the pedicle. This case is obviously not found in a local perforator-based propeller flap in clinical use. Therefore, the possible effect of a pedicle twist must also be evaluated in conjunction with active changes in vascular flow to accurately determine the role of arterial augmentation and/or reduction in venous flow resistance in perforator-based flaps. On the other hand, although our study points to certain directions to follow in the clinic to increase the survival rate of perforator-based flaps, ultimately only experience and ideally prospective clinical studies can define the role of active flow alterations in the perforator pedicle for the local propeller flap method in the practice of reconstructive surgery.

The clinical part of our work was mainly concerned with the actual, prospective and comprehensive evaluation of the results of perforator-based flap reconstruction in the calf performed by the doctoral student at the University Clinic of Plastic and Reconstructive Surgery of the University Hospital "Inselspital" in Bern. The results of this research showed for the first time in the literature related to propeller flaps in the calf a link between the source artery of the flap and the rate of postoperative complications, and was an important factor in the publication of these results in the renowned orthopaedic journal, Journal of Bone and Joint Surgery118. The fact that the fibular artery appears to be less safe as a source artery for propeller flaps is of course novel and has given rise to various discussions in the field. However, this study has also had a direct impact on day-to-day clinical practice in our unit. Thus, in patients with comorbidities and lateral defects in the distal third of the calf, we have reduced the indication for propeller flaps and prefer to approach other reconstructive solutions. On the other hand, posterior tibial artery perforator-based flaps are extremely robust and their use is recommended whenever calf defects lend themselves to this option.

Finally, we believe that we can state on the one hand that our work has succeeded in drawing some highly relevant conclusions in reconstructive surgery with perforator-based flaps, on the other hand it has obviously opened up new questions and research directions, hopefully being an important step in deepening the understanding of this surgical technique both experimentally and clinically.

5. BIBLIOGRAFIE

1. Aldea PA, Shaw WW. The evolution of the surgical management of severe lower extremity trauma. *Clin Plast Surg*. 1986;13(4):549-569.

2. Hippocrates., Adams F. *The Genuine Works of Hippocrates ; Translated from the Greek with a Preliminary Discourse and Annotations*. W. Wood; 1886. Accessed April 2, 2020. https://catalog.hathitrust.org/Record/009358009

3. The Apologie and Treatise of Ambroise Paré Containing the Voyages Made into Divers Places, with Many of His Writings upon Surgery. *Yale J Biol Med*. 1953;25(6):545.

4. Larrey DJ. *Mémoires de Chirurgie Militaire et Campagnes*. Chez J. Smith; 1812. Accessed April 2, 2020. https://catalog.hathitrust.org/Record/012241640

5. Lister J. ON A NEW METHOD OF TREATING COMPOUND FRACTURE, ABSCESS, ETC., WITH OBSERVATIONS ON THE CONDITIONS OF SUPPURATION. *The Lancet*. 1927;209(5406):773-775. doi:10.1016/S0140-6736(00)73482-9

6. Hauben DJ, Sonneveld GJ. The influence of war on the development of plastic surgery. *Ann Plast Surg*. 1983;10(1):65-69. doi:10.1097/00000637-198301000-00009

7. Higgins TF, Klatt JB, Beals TC. Lower Extremity Assessment Project (LEAP)--the best available evidence on limb-threatening lower extremity trauma. *Orthop Clin North Am*. 2010;41(2):233-239. doi:10.1016/j.ocl.2009.12.006

8. Werner CML, Pierpont Y, Pollak AN. The urgency of surgical débridement in the management of open fractures. *J Am Acad Orthop Surg*. 2008;16(7):369-375. doi:10.5435/00124635-200807000-00002

9. Godina M. Early microsurgical reconstruction of complex trauma of the extremities. *Plast Reconstr Surg*. 1986;78(3):285-292.

10. Karanas YL, Nigriny J, Chang J. The timing of microsurgical reconstruction in lower extremity trauma. *Microsurgery*. 2008;28(8):632-634. doi:10.1002/micr.20551

11. Byrd HS, Spicer TE, Cierney G. Management of open tibial fractures. *Plast Reconstr Surg*. 1985;76(5):719-730. doi:10.1097/00006534-198511000-00011

12. Hertel R, Lambert SM, Müller S, Ballmer FT, Ganz R. On the timing of soft-tissue reconstruction for open fractures of the lower leg. *Arch Orthop Trauma Surg*. 1999;119(1-2):7-12. doi:10.1007/s004020050346

13. Yaremchuk MJ, Brumback RJ, Manson PN, Burgess AR, Poka A, Weiland AJ. Acute and definitive management of traumatic osteocutaneous defects of the lower extremity. *Plast Reconstr Surg*. 1987;80(1):1-14. doi:10.1097/00006534-198707000-00001

14. Ong YS, Levin LS. Lower limb salvage in trauma. *Plast Reconstr Surg*. 2010;125(2):582-588. doi:10.1097/PRS.0b013e3181c82ed1

15. Giannoudis PV, Papakostidis C, Roberts C. A review of the management of open fractures of the tibia and femur. *J Bone Joint Surg Br*. 2006;88(3):281-289. doi:10.1302/0301-620X.88B3.16465

16. Miller-Thomas MM, West OC, Cohen AM. Diagnosing Traumatic Arterial Injury in the Extremities with CT Angiography: Pearls and Pitfalls. *RadioGraphics*. 2005;25(suppl_1):S133-S142. doi:10.1148/rg.25si055511

17. Seamon MJ, Smoger D, Torres DM, et al. A prospective validation of a current practice: the detection of extremity vascular injury with CT angiography. *J Trauma*. 2009;67(2):238-243; discussion 243-244. doi:10.1097/TA.0b013e3181a51bf9

18. Fitzgerald J, Michael E. Protocol for lower extremity trauma. *J Foot Ankle Surg*. 1995;34(1):2-11. doi:10.1016/S1067-2516(09)80095-1

19. Glass GE, Pearse MF, Nanchahal J. Improving lower limb salvage following fractures with vascular injury: a systematic review and new management algorithm. *J Plast Reconstr Aesthet Surg*. 2009;62(5):571-579. doi:10.1016/j.bjps.2008.11.117

20. Fowler J, Macintyre N, Rehman S, Gaughan JP, Leslie S. The importance of surgical sequence in the treatment of lower extremity injuries with concomitant vascular injury: A meta-analysis. *Injury*. 2009;40(1):72-76. doi:10.1016/j.injury.2008.08.043

21. Terzis JK, Sun DD, Thanos PK. Historical and basic science review: past, present, and future of nerve repair. *J Reconstr Microsurg*. 1997;13(3):215-225. doi:10.1055/s-2007-1006407

22. Desouches C, Alluin O, Mutaftschiev N, et al. [Peripheral nerve repair: 30 centuries of scientific research]. *Rev Neurol (Paris)*. 2005;161(11):1045-1059. doi:10.1016/s0035-3787(05)85172-0

23. Lange RH. Limb reconstruction versus amputation decision making in massive lower extremity trauma. *Clin Orthop Relat Res*. 1989;(243):92-99.

24. Song DH, Neligan PC. *Plastic Surgery: Lower Extremity, Trunk and Burns*. Elsevier Health Sciences; 2012.

25. Taylor GI, Miller GD, Ham FJ. The free vascularized bone graft. A clinical extension of microvascular techniques. *Plast Reconstr Surg*. 1975;55(5):533-544. doi:10.1097/00006534-197505000-00002

26. Parrett BM, Talbot SG, Pribaz JJ, Lee BT. A review of local and regional flaps for distal leg reconstruction. *J Reconstr Microsurg*. 2009;25(7):445-455. doi:10.1055/s-0029-1223847

27. May JW, Lukash FN, Gallico GG. Latissimus dorsi free muscle flap in lower-extremity reconstruction. *Plast Reconstr Surg*. 1981;68(4):603-607. doi:10.1097/00006534-198110000-00022

28. Georgescu AV, Ignatiadis I, Ileana M, Irina C, Filip A, Olariu R. Long-term results after muscle-rib flap transfer for reconstruction of composite limb defects. *Microsurgery*. 2011;31(3):218-222. doi:10.1002/micr.20857

29. Pederson WC, Grome L. Microsurgical Reconstruction of the Lower Extremity. *Semin Plast Surg*. 2019;33(1):54-58. doi:10.1055/s-0039-1677878

30. Saint-Cyr M, Schaverien M, Wong C, et al. The extended anterolateral thigh flap: anatomical basis and clinical experience. *Plast Reconstr Surg*. 2009;123(4):1245-1255. doi:10.1097/PRS.0b013e31819e2718

31. Hong JP, Sun SH, Ben-Nakhi M. Modified superficial circumflex iliac artery perforator flap and supermicrosurgery technique for lower extremity reconstruction: a new approach for moderate-sized defects. *Ann Plast Surg*. 2013;71(4):380-383. doi:10.1097/SAP.0b013e3182503ac5

32. Bhishagratna Kunjalal. *An English Translation of the Sushruta Samhita Based on Original Sanskrit Text.*; 1907. Accessed February 19, 2021. https://catalog.hathitrust.org/Record/100327008

33. An Account of Two Successful Operations for Restoring a Lost Nose (Lost Noses) from the Integuments of the Forehead, in the Cases of Two Officers in His Majesty's Army : To Which Are Affixed, Historical and Physiological Remarks on the Nasal Operation; Including Descriptions of the Indian and Italian Methods. *Med Chir J Rev*. 1817;4(23):376-387.

34. De Curtorum Chirurgia Per Insitionem by Tagliacozzi, Gaspare: Near Fine Hardcover (1996) Reprint Edition | Row By Row Bookshop. Accessed February 19, 2021. https://www.abebooks.co.uk/Curtorum-Chirurgia-Insitionem-Tagliacozzi-Gaspare-Classics/30303558108/bd

35. Manchot C. *Die Hautarterien des menschlichen Körpers.* Vogel; 1889.

36. Salmon M. *Artères de la peau.*; 1936.

37. Hamilton FH, Hamilton FH. *Elkoplasty, or, Anaplasty Applied to the Treatment of Old Ulcers : Also, A New Mode of Treatment for Delayed or Non-Union of a Fractured Humerus*. New York : Holman, Gray, & Co.; 1854. Accessed February 19, 2021. http://archive.org/details/66810110R.nlm.nih.gov

38. Filatov VP, Labunka M, Gnudi MT, Webster JP. Plastic Procedure Using a Round Pedicle. *Surgical Clinics of North America*. 1959;39(2):277-287. doi:10.1016/S0039-6109(16)35731-0

39. Gillies HD. THE TUBED PEDICLE IN PLASTIC SURGERY. *The Lancet*. 1920;196(5058):320. doi:10.1016/S0140-6736(01)18742-8

40. Ger R. The technique of muscle transposition in the operative treatment of traumatic and ulcerative lesions of the leg. *J Trauma*. 1971;11(6):502-510. doi:10.1097/00005373-197106000-00007

41. McGregor IA, Jackson IT. The groin flap. *British Journal of Plastic Surgery*. 1972;25:3-16. doi:10.1016/S0007-1226(72)80003-1

42. Daniel RK, Taylor GI. Distant transfer of an island flap by microvascular anastomoses. A clinical technique. *Plast Reconstr Surg*. 1973;52(2):111-117. doi:10.1097/00006534-197308000-00001

43. McCraw JB. The recent history of myocutaneous flaps. *Clin Plast Surg*. 1980;7(1):3-7.

44. Mathes SJ, Nahai F. Classification of the vascular anatomy of muscles: experimental and clinical correlation. *Plast Reconstr Surg*. 1981;67(2):177-187.

45. Godina M, Lister G. The Tailored Latissimus Dorsi Free Flap. *Plastic and Reconstructive Surgery*. 1987;80(2):304-306.

46. Banic A, Wulff K. Latissimus dorsi free flaps for total repair of extensive lower leg injuries in children. *Plast Reconstr Surg*. 1987;79(5):769-775. doi:10.1097/00006534-198705000-00016

47. Pontén B. The fasciocutaneous flap: its use in soft tissue defects of the lower leg. *Br J Plast Surg*. 1981;34(2):215-220. doi:10.1016/s0007-1226(81)80097-5

48. Taylor GI, Palmer JH. The vascular territories (angiosomes) of the body: experimental study and clinical applications. *Br J Plast Surg*. 1987;40(2):113-141. doi:10.1016/0007-1226(87)90185-8

49. Koshima I, Soeda S. Inferior epigastric artery skin flaps without rectus abdominis muscle. *Br J Plast Surg*. 1989;42(6):645-648.

50. Taylor GI, Doyle M, McCarten G. The Doppler probe for planning flaps: anatomical study and clinical applications. *Br J Plast Surg*. 1990;43(1):1-16. doi:10.1016/0007-1226(90)90039-3

51. Song YG, Chen GZ, Song YL. The free thigh flap: a new free flap concept based on the septocutaneous artery. *Br J Plast Surg*. 1984;37(2):149-159. doi:10.1016/0007-1226(84)90002-x

52. Wei F, Jain V, Celik N, Chen H, Chuang DC-C, Lin C. Have we found an ideal soft-tissue flap? An experience with 672 anterolateral thigh flaps. *Plast Reconstr Surg*. 2002;109(7):2219-2226; discussion 2227-2230. doi:10.1097/00006534-200206000-00007

53. Hyakusoku H, Yamamoto T, Fumiiri M. The propeller flap method. *Br J Plast Surg*. 1991;44(1):53-54.

54. Hallock GG. The propeller flap version of the adductor muscle perforator flap for coverage of ischial or trochanteric pressure sores. *Ann Plast Surg*. 2006;56(5):540-542. doi:10.1097/01.sap.0000210512.81988.2b

55. Teo TC. The propeller flap concept. *Clin Plast Surg*. 2010;37(4):615-626, vi. doi:10.1016/j.cps.2010.06.003

56. Georgescu AV. Propeller Perforator Flaps in Distal Lower Leg: Evolution and Clinical Applications. *Arch Plast Surg*. 2012;39(2):94-105. doi:10.5999/aps.2012.39.2.94

57. Pignatti M, Ogawa R, Hallock GG, et al. The "Tokyo" consensus on propeller flaps. *Plast Reconstr Surg*. 2011;127(2):716-722. doi:10.1097/PRS.0b013e3181fed6b2

58. Taylor GI, Pan WR. Angiosomes of the leg: anatomic study and clinical implications. *Plast Reconstr Surg*. 1998;102(3):599-616; discussion 617-618.

59. Morris SF, Tang M, Almutari K, Geddes C, Yang D. The anatomic basis of perforator flaps. *Clin Plast Surg*. 2010;37(4):553-570, xi. doi:10.1016/j.cps.2010.06.006

60. Saint-Cyr M, Wong C, Schaverien M, Mojallal A, Rohrich RJ. The perforasome theory: vascular anatomy and clinical implications. *Plast Reconstr Surg*. 2009;124(5):1529-1544. doi:10.1097/PRS.0b013e3181b98a6c

61. Geddes CR, Tang M, Yang D, Morris SF. Anatomy of the Integument of the Lower Extremity. In: *Perforator Flaps Anatomy, Technique, & Clinical Applications Second Edition*. ; :667-705.

62. Acland RD, Schusterman M, Godina M, Eder E, Taylor GI, Carlisle I. The saphenous neurovascular free flap. *Plast Reconstr Surg*. 1981;67(6):763-774. doi:10.1097/00006534-198106000-00009

63. Shaw AD, Ghosh SJ, Quaba AA. The island posterior calf fasciocutaneous flap: an alternative to the gastrocnemius muscle for cover of knee and tibial defects. *Plast Reconstr Surg*. 1998;101(6):1529-1536. doi:10.1097/00006534-199805000-00016

64. Hallock GG. Anatomic basis of the gastrocnemius perforator-based flap. *Ann Plast Surg*. 2001;47(5):517-522. doi:10.1097/00000637-200111000-00008

65. Morrison WA, Shen TY. Anterior tibial artery flap: anatomy and case report. *Br J Plast Surg*. 1987;40(3):230-235. doi:10.1016/0007-1226(87)90115-9

66. Masquelet AC, Beveridge J, Romana C, Gerber C. The lateral supramalleolar flap. *Plast Reconstr Surg*. 1988;81(1):74-81. doi:10.1097/00006534-198801000-00014

67. Georgescu AV, Matei IR, Bumbasirevic M, Soucacos PN. Why, when and how propeller perforator flaps in reconstructive surgery. *Injury*. 2019;50 Suppl 5:S3-S7. doi:10.1016/j.injury.2019.10.037

68. Georgescu AV, Matei IR, Capota IM. The use of propeller perforator flaps for diabetic limb salvage: a retrospective review of 25 cases. *Diabet Foot Ankle*. 2012;3. doi:10.3402/dfa.v3i0.18978

69. Gokrem S, Sarifakioğlu N, Toksoy K, Terzioğlu A, Aslan G. Effects of 360-degree pedicle torsion on island skin flaps: experimental study in rats. *J Reconstr Microsurg*. 2005;21(5):313-316. doi:10.1055/s-2005-871773

70. Donski PK, Fogdestam I. Distally based fasciocutaneous flap from the sural region. A preliminary report. *Scand J Plast Reconstr Surg*. 1983;17(3):191-196. doi:10.3109/02844318309013118

71. Taylor GI, Corlett RJ, Dhar SC, Ashton MW. The anatomical (angiosome) and clinical territories of cutaneous perforating arteries: development of the concept and designing

safe flaps. *Plast Reconstr Surg.* 2011;127(4):1447-1459. doi:10.1097/PRS.0b013e318208d21b

72. Shafighi M, Olariu R, Fathi AR, et al. Dimethyloxalylglycine stabilizes HIF-1α in cultured human endothelial cells and increases random-pattern skin flap survival in vivo. *Plast Reconstr Surg.* 2011;128(2):415-422. doi:10.1097/PRS.0b013e31821e6e69

73. Shafighi M, Olariu R, Brun C, et al. The role of androgens on hypoxia-inducible factor (HIF)-1α-induced angiogenesis and on the survival of ischemically challenged skin flaps in a rat model. *Microsurgery.* 2012;32(6):475-481. doi:10.1002/micr.21996

74. Blondeel PN, Van Landuyt KHI, Monstrey SJM, et al. The "Gent" consensus on perforator flap terminology: preliminary definitions. *Plast Reconstr Surg.* 2003;112(5):1378-1383; quiz 1383, 1516; discussion 1384-1387. doi:10.1097/01.PRS.0000081071.83805.B6

75. Ayestaray B, Ogawa R, Ono S, Hyakusoku H. Propeller flaps: classification and clinical applications. *Ann Chir Plast Esthet.* 2011;56(2):90-98. doi:10.1016/j.anplas.2010.11.004

76. Quaba O, Quaba A. Pedicled Perforator Flaps for the Lower Limb. *Seminars in Plastic Surgery.* 2006;20(2):103-111. doi:10.1055/s-2006-941717

77. Bekara F, Herlin C, Somda S, de Runz A, Grolleau JL, Chaput B. Free versus perforator-pedicled propeller flaps in lower extremity reconstruction: What is the safest coverage? A meta-analysis. *Microsurgery.* Published online March 28, 2016. doi:10.1002/micr.30047

78. Nelson JA, Fischer JP, Brazio PS, Kovach SJ, Rosson GD, Rad AN. A review of propeller flaps for distal lower extremity soft tissue reconstruction: Is flap loss too high? *Microsurgery.* 2013;33(7):578-586. doi:10.1002/micr.22134

79. Bekara F, Herlin C, Mojallal A, et al. A Systematic Review and Meta-Analysis of Perforator-Pedicled Propeller Flaps in Lower Extremity Defects: Identification of Risk Factors for Complications. *Plast Reconstr Surg.* 2016;137(1):314-331. doi:10.1097/PRS.0000000000001891

80. Tanaka Y, Tajima S. The influence of arterial inflow and venous outflow on the survival of reversed-flow island flaps: an experimental study. *Plast Reconstr Surg.* 1997;99(7):2021-2029.

81. Hallock GG, Rice DC. Efficacy of venous supercharging of the deep inferior epigastric perforator flap in a rat model. *Plast Reconstr Surg.* 2005;116(2):551-555; discussion 556.

82. Groth AK, Campos ACL, Gonçalves CG, et al. Effects of venous supercharging in deep inferior epigastric artery perforator flap. *Acta Cir Bras.* 2007;22(6):474-478.

83. Yamamoto Y, Sakurai H, Nakazawa H, Nozaki M. Effect of vascular augmentation on the haemodynamics and survival area in a rat abdominal perforator flap model. *J Plast Reconstr Aesthet Surg.* 2009;62(2):244-249. doi:10.1016/j.bjps.2007.11.078

84. Gümüş N, Erkan M, Erçöçen AR. Vascular pressure monitorization for necessity of vascular augmentation in a rat extended abdominal perforator flap model. *Microsurgery.* 2012;32(4):303-308. doi:10.1002/micr.21952

85. Coşkunfirat OK, Islamoğlu K, Ozgentaş HE. Posterior thigh perforator-based flap: a new experimental model in rats. *Ann Plast Surg*. 2002;48(3):286-291.

86. Tim CR, Martignago CCS, da Silva VR, et al. A Comparison of Three Methods for the Analysis of Skin Flap Viability: Reliability and Validity. *Adv Wound Care (New Rochelle)*. 2018;7(5):157-163. doi:10.1089/wound.2017.0758

87. Chang H, Nobuaki I, Minabe T, Nakajima H. Comparison of three different supercharging procedures in a rat skin flap model. *Plast Reconstr Surg*. 2004;113(1):277-283. doi:10.1097/01.PRS.0000095953.57320.2F

88. Chen W, Li Y-Q, Tang Y, et al. [Which vessel, the artery or the vein is more important in vascular supercharge: an investigation of vascular changes on rat abdominal supercharging flap models]. *Zhonghua Zheng Xing Wai Ke Za Zhi*. 2013;29(1):40-44.

89. Sano K, Hallock GG, Rice DC. Venous "supercharging" augments survival of the delayed rat TRAM flap. *Ann Plast Surg*. 2003;51(4):398-402. doi:10.1097/01.SAP.0000068111.83104.7F

90. Zheng J, Xi S, Ding M, et al. Effects of Venous Superdrainage and Arterial Supercharging on Dorsal Perforator Flap in a Rat Model. *PLOS ONE*. 2016;11(8):e0160942. doi:10.1371/journal.pone.0160942

91. Callegari PR, Taylor GI, Caddy CM, Minabe T. An anatomic review of the delay phenomenon: I. Experimental studies. *Plast Reconstr Surg*. 1992;89(3):397-407; discussion 417-418.

92. Dhar SC, Taylor GI. The delay phenomenon: the story unfolds. *Plast Reconstr Surg*. 1999;104(7):2079-2091.

93. Taylor GI, Corlett RJ, Ashton MW. The Functional Angiosome: Clinical Implications of the Anatomical Concept. *Plast Reconstr Surg*. 2017;140(4):721-733. doi:10.1097/PRS.0000000000003694

94. Seyhan T, Deniz M, Borman H, Ulusal Güzel B, Cağlar B. Comparison of two different vascular delay methods in a rat cranial epigastric perforator flap model. *Ann Plast Surg*. 2010;64(1):89-92. doi:10.1097/SAP.0b013e3181951720

95. D'Arpa S, Toia F, Pirrello R, Moschella F, Cordova A. Propeller Flaps: A Review of Indications, Technique, and Results. *BioMed Research International*. 2014;2014:986829. doi:10.1155/2014/986829

96. Blondeel PN, Morris SF, Hallock GG, Neligan PC. *Perforator Flaps: Anatomy, Technique, & Clinical Applications, Second Edition*. CRC Press; 2013.

97. Rad AN, Singh NK, Rosson GD. Peroneal artery perforator-based propeller flap reconstruction of the lateral distal lower extremity after tumor extirpation: case report and literature review. *Microsurgery*. 2008;28(8):663-670. doi:10.1002/micr.20557

98. Innocenti M, Menichini G, Baldrighi C, Delcroix L, Vignini L, Tos P. Are there risk factors for complications of perforator-based propeller flaps for lower-extremity reconstruction? *Clin Orthop Relat Res*. 2014;472(7):2276-2286. doi:10.1007/s11999-014-3537-6

99. Blondeel PN, Beyens G, Verhaeghe R, et al. Doppler flowmetry in the planning of perforator flaps. *Br J Plast Surg*. 1998;51(3):202-209.

100. Koshima I, Moriguchi T, Ohta S, Hamanaka T, Inoue T, Ikeda A. The vasculature and clinical application of the posterior tibial perforator-based flap. *Plast Reconstr Surg*. 1992;90(4):643-649.

101. Tanaka K, Matsumura H, Miyaki T, Watanabe K. An anatomic study of the intermuscular septum of the lower leg; branches from the posterior tibial artery and potential for reconstruction of the lower leg and the heel. *J Plast Reconstr Aesthet Surg*. 2006;59(8):835-838. doi:10.1016/j.bjps.2005.10.020

102. Acland RD. Refinements in lower extremity free flap surgery. *Clin Plast Surg*. 1990;17(4):733-744.

103. Artiaco S, Battiston B, Colzani G, et al. Perforator Based Propeller Flaps in Limb Reconstructive Surgery: Clinical Application and Literature Review. *BioMed Research International*. 2014;2014:690649. doi:10.1155/2014/690649

104. Yazar S, Lin C-H, Lin Y-T, Ulusal AE, Wei F-C. Outcome comparison between free muscle and free fasciocutaneous flaps for reconstruction of distal third and ankle traumatic open tibial fractures. *Plast Reconstr Surg*. 2006;117(7):2468-2475; discussion 2476-2477. doi:10.1097/01.prs.0000224304.56885.c2

105. Gunnarsson GL, Jackson IT, Westvik TS, Thomsen JB. The freestyle pedicle perforator flap: a new favorite for the reconstruction of moderate-sized defects of the torso and extremities. *Eur J Plast Surg*. 2015;38:31-36. doi:10.1007/s00238-014-1043-4

106. Karki D, Narayan RP. The versatility of perforator-based propeller flap for reconstruction of distal leg and ankle defects. *Plast Surg Int*. 2012;2012:303247. doi:10.1155/2012/303247

107. Mateev MA, Kuokkanen HOM. Reconstruction of soft tissue defects in the extremities with a pedicled perforator flap: series of 25 patients. *J Plast Surg Hand Surg*. 2012;46(1):32-36. doi:10.3109/2000656X.2011.634562

108. Georgescu AV, Matei I, Ardelean F, Capota I. Microsurgical nonmicrovascular flaps in forearm and hand reconstruction. *Microsurgery*. 2007;27(5):384-394. doi:10.1002/micr.20376

109. Yu S, Zang M, Xu L, et al. Perforator Propeller Flap for Oncologic Reconstruction of Soft Tissue Defects in Trunk and Extremities. *Ann Plast Surg*. 2016;77(4):456-463. doi:10.1097/SAP.0000000000000649

110. Ignatiadis IA, Georgakopoulos GD, Tsiampa VA, Polyzois VD, Arapoglou DK, Papalois AE. Distal posterior tibial artery perforator flaps for the management of calcaneal and Achilles tendon injuries in diabetic and non-diabetic patients. *Diabet Foot Ankle*. 2011;2. doi:10.3402/dfa.v2i0.7483

111. Schaverien MV, Hamilton SA, Fairburn N, Rao P, Quaba AA. Lower limb reconstruction using the islanded posterior tibial artery perforator flap. *Plast Reconstr Surg*. 2010;125(6):1735-1743. doi:10.1097/PRS.0b013e3181ccdc08

112. Jakubietz RG, Jakubietz MG, Gruenert JG, Kloss DF. The 180-degree perforator-based propeller flap for soft tissue coverage of the distal, lower extremity: a new method to achieve reliable coverage of the distal lower extremity with a local, fasciocutaneous perforator flap. *Ann Plast Surg*. 2007;59(6):667-671. doi:10.1097/SAP.0b013e31803c9b66

113. Erdmann MW, Court-Brown CM, Quaba AA. A five year review of islanded distally based fasciocutaneous flaps on the lower limb. *Br J Plast Surg*. 1997;50(6):421-427.

114. Masia J, Moscatiello F, Pons G, Fernandez M, Lopez S, Serret P. Our experience in lower limb reconstruction with perforator flaps. *Ann Plast Surg*. 2007;58(5):507-512. doi:10.1097/01.sap.0000239841.47088.a5

115. Tos P, Innocenti M, Artiaco S, et al. Perforator-based propeller flaps treating loss of substance in the lower limb. *Journal of Orthopaedics and Traumatology : Official Journal of the Italian Society of Orthopaedics and Traumatology*. 2011;12(2):93-99. doi:10.1007/s10195-011-0136-0

116. Jiga LP, Barac S, Taranu G, et al. The versatility of propeller flaps for lower limb reconstruction in patients with peripheral arterial obstructive disease: initial experience. *Ann Plast Surg*. 2010;64(2):193-197. doi:10.1097/SAP.0b013e3181a72f8c

117. Olariu R, Moser HL, Lese I, et al. The effects of optimizing blood inflow in the pedicle on perforator flap survival: A pilot study in a rat model. *Arch Plast Surg*. 2020;47(3):209-216. doi:10.5999/aps.2019.00871

118. Lese I, Grobbelaar AO, Sabau D, Georgescu AV, Constantinescu MA, Olariu R. The Propeller Flap for Traumatic Distal Lower-Limb Reconstruction: Risk Factors, Pitfalls, and Recommendations. *J Bone Joint Surg Am*. 2020;102(6):510-518. doi:10.2106/JBJS.19.00648