Management of microanastomosis in patients affected by vessel diseases

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Abstract. – OBJECTIVE: In the last 10 years with the advances in microsurgery of techniques and materials the indications for free tissue transfer have considerably been increased. But, there are still some limitations and drawbacks. Among risk factors associated with flap failure, atherosclerosis can affect both the flap and the recipient vessels of free microvascular tissue transfers. The purpose of this paper is to discuss about the pathogenesis of Monckeberg's sclerosis, and the topics that must be taken into consideration when performing microsurgery in these patients.

METHODS: PubMed database was searched using Mesh. The following terms was added to the search builder: Monckeberg's sclerosis, free flap. The Boolean operator "AND" was selected. All the selectable Mesh headings for "Monckeberg's sclerosis" and "free flap" were included.

RESULTS: Almost all the literature works about microsurgery in Monckeberg's sclerosis patient show the importance of an accurate preoperative and postoperative evaluation and of a proper surgical technique.

CONCLUSIONS: When adequate preoperative evaluation, surgical technique and postoperative monitoring are performed, even severe atherosclerosis should not be considered an absolute contraindication for microvascular surgery.

Key Words:

Microsurgery, Monckeberg's sclerosis, Free flap.

Introduction

Microsurgery was made possible in the late nineteenth and early twentieth centuries when technology allowed development of operative microscope, micro-instruments and micro-sutures¹⁻³. It started as an advanced surgical technique transforming what was once thought of as a miracle into reality. Then different disciplines have been brought together in the "world of microsurgery" allowing for the transfer of well-vas-

cularized tissue to defects in a single-stage procedure, and leading to improved quality of life. As a consequence of microsurgery human anatomy has been re-evaluated in the search for donor tissues vessels suitable for free tissue transfer.

In the last 10 years the indications for free tissue transfer have been increased involving, for example, children, elderly patients and even patients with complex medical conditions as hematologic disorders⁴. However, despite its universal popularity and wide of use in practice, there are still some limitations and drawbacks. Risk factors associated with flap failure rates include obesity, age⁵⁻⁹, previous irradiation^{10,11}, diabetes mellitus¹², smoking¹³, and systemic vascular disease¹⁴. Atherosclerosis is the most common risk factor for systemic vascular disease, and can affect both the flap vessels and the recipient vessels of free microvascular tissue transfers14. Patient selection, type of microsurgical technique, and postoperative care are more important in patients with pathology of layers of vessels. This paper studies the pathogenesis of atherosclerosis (ATS), and its subtype Monckeberg's sclerosis (MS), and the topics that must be taken into consideration when performing microsurgery in these patients.

Pathogenesis of Atherosclerosis and Monckeberg's Sclerosis

ATS is a degenerative disease that begins in early childhood and advances with age. The early lesions, so-called "fatty streaks," are small deposits of clearly vacuolated, lipid-containing cells called "foam cells" in the intima layer of vessels. These lesions are usually located in the aorta of infants and children¹⁴. Atherosclerotic vascular disease is a multifactorial process characterized by plaque formation seen in adults. These are categorized into three forms: gelatinous, fibrous, and complicated. Plaque formation begins with the gelatinous type, and fibrous changes occur around the plaque core over time; eventually, the lesion

becomes a fibrous plaque. Advanced plaques can be complicated by calcification, ulceration, hemorrhage, and necrosis¹⁴, In addition to genetic susceptibility, cholesterol levels, elevated blood pressure, diabetes mellitus, and cigarette smoking are the most important risk factors for the development of atherosclerosis¹⁴. Advanced atherosclerotic lesions partially or totally occlude the arteries, and fissures in these lesions lead to thrombosis, embolism, and aneurysmal dilatation. Advanced lesions are prone to rupture, and can easily undergo thrombosis⁴⁻⁹.

Monkemberg sclerosis, also called focal calcification, is a type of atherosclerosis that is more common in people over 50. It involves degeneration of smooth muscle cell (medial layer) followed by calcium deposition in the small and medium sized muscular arteries^{15,16} (Figures 1 A, B). It is mainly located in the lower and upper extremities and the arterial supply of the genital tract. Since the condition does not involve primarily the intimal layer of the artery, the lumen is kept open by the rigid media and, therefore, luminal narrowing is not a direct consequence^{15,16}. Recent studies, however, have demonstrated that MS is a risk factor for cardiovascular disease and peripheral artery obstruction. The exact etiopathogenesis of this process is far from being understood, but is frequently related to glucose intolerance, aging, male gender, autonomic neuropathy, osteoporosis and chronic renal failure.

Management of Sclerotic Vessels

However, microsurgery can be safely performed in both AS and MS patients after proper

evaluation and adaptation of a systemic approach. Patients should be evaluated thoroughly and dealt with at three stages: preoperative, intraoperative and postoperative.

Preoperative Stage

All patients destined to receive a free flap transfer for reconstruction of the extremities or head and neck region, should receive preoperative evaluation of the vasculature. First of all an accurate anamnesis and family history evaluation; it is important to assess whether patients present other diseases or sympthoms related to the MS. Then the vasculature is evaluated with imaging exams. This can be performed with color Doppler, which is the first exam required and eventually with arteriograms. However, magnetic resonance angiography or computed tomography (CT) angiograms are useful radiological procedures for the study of the peripheral vasculature, with minimal morbidity associated with the studies^{14,17-25}. During preoperative planning, flap type, pedicle length, and pedicle caliber should be judged properly so that there are no unanticipated steps, and so that microsurgical techniques can be performed comfortably and safely. To minimize unsatisfactory results, and to minimize the length of the surgical procedure, flaps having a constant anatomy and a long and large vascular pedicle should be chosen.

Generally, flap selection has to consider that flaps based on pedicle of upper limbs or from the central part of the body are less affected by pathology of vessels wall than those from the lower limbs or distal parts of the body¹⁴. Further-

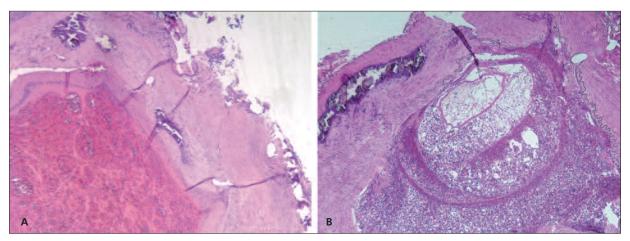


Figure 1. Histological evaluation of Mockemberg sclerosis showing degeneration of smooth muscle cell (medial layer) and calcium deposition in the small and medium sized muscular arteries. (Eosin-Hematoxylin stain. **A**, 2.5× magnification; **B**, 5× magnification).

more, recipient vessel selection depends on the site of reconstruction. Generally, vessels with a good caliber, located far from radiated and traumatized sites, are preferred²⁶⁻²⁹. Healthy vessels should be looked for and used. Flap pedicle length is also established in relation of the recipient vessel location²⁶⁻²⁹. The caliber and pulsation of the artery should be satisfactory for microvascular anastomosis.

Operative Stage

The operative stage is equally important. Severe atherosclerosis makes recipient vessels very vulnerable to traumatic injury and for this reason careful dissection is recommended. The vessels should be dissected adequately to provide for a safe anastomosis. All side branches should be ligated with extreme care. The operator has to ascertain that the suitable artery must have good pulsatile bleeding upon division.

Microscope is essential to best visualize vessels and their structure.

Irrigation with heparinized saline (100 U/ml) is always performed^{14,30-35}, and the lumen is checked for the presence of thrombi, atherosclerotic plaques or calcium deposition on a high magnification.

Very fine instruments, in well-trained hands, should avoid intimal damage. Flap dissection is followed by a time of flap perfusion for at least 15-20 minutes. The flap vessels are not handled during this time and are bathed with warm irrigating solution and 2% plain lidocaine. This procedure allows to relieve vessel spasm and to equilibrate flow dynamics in the flap.

If the vessel is divided when it is in spasm, after anastomosis it will also be in spasm.

Usually, pedicle division consists on clamping flap artery and then the vein.

If the vein is clamped first, the continuing inflow causes the flap vein to bulge, which may cause a severe vessel size discrepancy but may also avoid accidental vessel twisting at the time of anastomosis. Perfusion of the dissected flap with prepared tissue preservation solutions is never necessary prior to transfer.

When everything is ready the flap vessels are divided at the recipient site, to minimize blood flow interruption of the recipient vessels.

The status of the recipient vessels should be carefully verified just before division of the flap vessels.

Preparation of the vessel ends consists on: stripping the adventitia up to the area which would be

in the clamps, applying double clamps (single clamps may also be used during this step), taking care not to snap the clamp onto the vessel.

Since a frequent irrigation with saline solution is recommended, a moist sponge is placed beneath the vessel set-up in order to elevate the plane of the anastomosis and to provide a space for fluid to collect in before reaching the plane of the anastomosis and interfering with the field. Background material is placed beneath the clamp and vessels. Fine trimming with microscissors is performed to clearly see the vessel ends while suturing, and to prevent the adventitia from getting caught in the lumen while tying the knot. Adventitia inside the anastomosis can induce thrombus formation. The double clamps are approximated until the vessel ends just touch each other (neither tension nor vessel redundancy). Blood in the lumen beyond the clamps towards the open end must always be flushed out. Blood in undamaged vessels not in contact with wound thromboplastins does not clot and hence special precautions are not needed for the blood in the vessels beyond the clamps. Good hemostasis in the microsurgical field has to be guaranteed before starting the anastomosis. Some useful maneuvers can facilitate the microvascular anastomosis in atherosclerotic vessels.

- To inspect with the microscope and to palpate the recipient vessel, before choosing the best location of the anastomosis;
- To avoid vessel wall collapse, making a small area of excision;
- Carefully avoid to create a false lumen, when cutting the vessel, which may cause thrombosis.

Therefore, after cutting the artery, the atherosclerotic plaque should be carefully looked for, and the cut edge should be trimmed using fine scissors. It is important to select the appropriate clamps that do not put too much pressure on the vessel. Excessive tension can create fractures in the plaque or can induce damage to the vessel wall. Vessel loops can be used on the proximal and distal aspect of larger vessels if necessary. A round needle must be used to avoid damage to the intima. The size of the needle and suture can be a factor in the success of the anastomosis. It is preferable to perform interrupted sutures as this allows for perfect placement of the needle with every bite^{36,37} (Figure 1A). Additionally, it allows the surgeon to see the intima and make sure that it is included with every bite. Separation of the intima from the rest of the vessel wall must be avoided making sutures that passed from the inside of the lumen of the atherosclerotic vessel to the outside. Double needle suture can help in case of both ends of the vessels have plaque. Gentle handling of the vessels is extremely important and every move should be purposeful and accurate without ever placing the instruments into the vessels blindly. However, small needles may be inadequate to pierce calcium deposition in the intima. Vessel dilation is dangerous and should be performed with extreme care only if necessary¹⁴. Eversion of the vessel walls avoids leaving raw surfaces exposed to blood flow. During the anastomosis the surgeon has to visualize the lumen with each bite. It is useful, tying the last 3-4 sutures at the end of anastomosis. The sutures should be tied without too much tension, as tension can cause erosion into the plaque and tearing of the vessel wall. Manipulation of the flap after anastomosis is possible at least after 10 min from the end of the anastomosis, to avoid creating turbulence and/or damage to the vessel wall and to allow invisible microthrombi to be washed out or become more stable¹⁴.

Before wound closure, it should be ensured that there is no pressure on the vessels or kinking of the pedicle. Both end-to-end and end-to-side anastomoses are practicable in atherosclerotic patients. However, careful thought must be given during decision-making. Several reports showed no difference in success rates between end-to-end and end-to-side anastomoses when evaluating a large group of flaps^{14,38-40}.

In patient with MS L-T anastomosis are preferred, using simple interrupted suture technique. Moreover, the use a larger caliber suture allows to pass through the rigid wall more easily. During the anastomosis phase, irrigation with pure heparin is performed and vessels are cleaned from the crystals, that are located in the medial layer of vessel, with a No 5 jeweler's forceps (Figure 2).

Postoperative Stage

Postoperative care of free tissue transfer patients requires that patients be adequately hydrated. Maintenance of proper body temperature and hematocrit is also important. Preoperative anticoagulation is not used by many surgeons³⁵. There is no consensus on anticoagulation after free tissue transfer^{41,42}. The main agents include heparin, dextran, aspirin, and ketorolac. Only a minority of the surgeons don't use any anticoagulant³⁵.

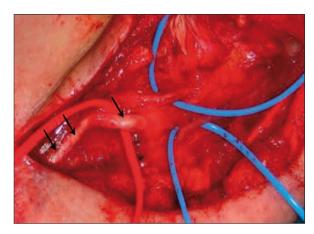


Figure 2. Preoperative figure showing arterial calcification.

Our regimen for the anticoagulation protocol for such situations cares is to maintain < 30 HTC with 30-50 cc/kg of fluid therapy, 500 cc of dextran 40%, 50-100 UI/kg heparin in elastomer for 5 days.

Flap monitoring is similar to flaps performed in nonatherosclerotic patients. In addition to clinical examination, Doppler ultrasonography and temperature monitoring are practical methods for postoperative monitoring. Doppler ultrasound, which is the most widely used, offers an ease of use, cost effectiveness, and ease of interpretation. Implantable Doppler devices offer similar advantages but are invasive and are not widely used. Temperature probes are less reliable due to the environmental influence but remain an important adjunct to clinical observation⁴³. Laser Doppler, the infusion of radioactive tracers⁴⁴, hydrogen gas⁴⁵, and fluorescein⁴⁶, as well as temperature measurements⁴⁷ and photoplethysmography are others less commonly used methods of monitoring tissue perfusion.

Patients operated on the lower extremity are not allowed to ambulate postoperatively for a minimum of two weeks. The inosculation and the healing of the flap to the wound bed, the selection of muscle or skin, and the "take" of the skin graft, are determinant for the dependency of the lower extremity. Those patients that have reconstruction around the foot and ankle are most prone to arise venous pressure and to a resultant edema of the flap. This edema can result in the dehiscence of the free flap from the surrounding tissue bed. For this reason, patients are required to keep their limbs elevated, need mild compressive garments and undergo bed to chair transfer for a minimum of two weeks.

Even for reconstruction cases not requiring a skin component, a portion of the free flap's skin may be exteriorized and may be used to evaluate its perfusion by monitoring the skin temperature, capillary refill, turgor, color, and bleeding. This skin paddle technique is one of the most accurate and reliable ways to evaluate flap perfusion. It allows the surgeon to monitor for both arterial insufficiency as well as venous obstruction. Arterial insufficiency is present when the skin becomes pale and cool and fails to bleed after a needle stick. Venous congestion usually results in edema and darkening of the skin color. During early venous obstruction, a needle stick will cause rapid bleeding of dark blood. To improve the reliability of a monitoring component of a flap, it is recommended that its size be larger than 1-2 cm. This allows enough perforating vessels to make correlation to the vascular pedicle^{48,49}. The perforator to this skin paddle should have an appropriate caliber while avoiding any torsion or tension during the inset of the flap. The reported sensitivity of the monitoring flap to detect a vascular occlusion is 100% with a 36% false-positive rate. However, early signs of a vascular compromise may be subtle and require an experienced examiner to recognize them. Therefore, clinical observation is still indispensable in monitoring flaps^{48,49}.

Conclusions

Pathology of wall of vessels are common diseases, especially in older individuals, and they affects the success of microsurgical procedures. Atherosclerotic patients should be evaluated carefully before microsurgery, to avoid possible complications. For this reason a meticulous vascular study is required.

During the operative phase, complications can be reduced if various technical details are respected by surgeons. The postoperative period also requires precise monitoring to obtain the maximum benefit from surgery. However, in cases of MS, the rules for each surgical step and the requirements for delicate and fine work are more strict than those for normal individuals. If a patient's medical problems do not constitute an handicap, and when proper surgical technique is performed, even severe atherosclerosis should not be considered a contraindication for microvascular surgery.

Conflict of Interest

All authors hereby declare not to have any potential conflict of interests and not to have received funding for this work from any organizations.

References

- NYLEN CO. The microscope in aural surgery: Its first use and later development. Acta Otolaryngol Suppl 1954; 116: 226-240.
- WIDSTRAND A, ED. Svenska Laekare i ord och bild-Portraetgalleri med biografi ska uppgifler oever nu levande svenska laekare. Stockholm, Sweden: Biografiskt Galleri A-B; 1939.
- STAHLE J. Carl Olof Nylen (1892-1978): Den foerste att tillaempa otomikroskopi. Sven Oenh-Tidskr 2005; 3: 44.
- 4) OZKAN O, CHEN HC, MARDINI S, CIGNA E, HAO SP, HUNG KF, CHEN HS. Microvascular free tissue transfer in patients with hematological disorders. Plast Reconstr Surg 2006; 118: 936-944.
- SHESTAK KC, JONES NF. Microsurgical free-tissue transfer in the elderly patient. Plast Reconstr Surg 1991; 88: 259-263.
- BONAWITZ SC, SCHNARRS RH, ROSENTHAL AI, ROGERS GK, NEWTON ED. Free-tissue transfer in elderly patients. Plast Reconstr Surg 1991; 87: 1074-1079
- SERLETTI JM, HIGGINS JP, MORAN S, ORLANDO GS. Factors affecting outcome in free tissue transfer in the elderly. Plast Reconstr Surg 2000; 106: 66-70.
- 8) MALATA CM, COOTER RD, BATCHELOR AG, SIMPSON KH, BROWNING FS, KAY SP. Microvascular free-tissue transfers in elderly patients: The leeds experience. Plast Reconstr Surg 1996; 98: 1234-1241.
- OZKAN O, OZGENTAS HE, ISLAMOGLU K, BOZTUG N, BI-GAT Z, DIKICI MB. Experiences with microsurgical tissue transfers in elderly patients. Microsurgery 2005; 25: 390-395.
- CLARKE HM, HOWARD CR, PYNN BR, McKEE NH. Delayed neovascularization in free skin flap transfer to irradiated beds in rats. Plast Reconstr Surg 1985; 75: 560-564.
- Doyle JW, Li YQ, Salloum A, FitzGerald TJ, Walton RL. The effects of radiation on neovascularization in a rat model. Plast Reconstr Surg 1996; 98: 129-135.
- 12) VALENTINI V, CASSONI A, MARIANETTI TM, MITRO V, GENNARO P, IALONGO C, IANNETTI G. Diabetes as main risk factor in head and neck reconstructive surgery with free flaps. J Craniofac Surg 2008; 19: 1080-1108.
- 13) VAN ADRICHEM LN, HOEGEN R, HOVIUS SE, KORT WJ, VAN STRIK R, VUZEVSKI VD, VAN DER MEULEN JC. The effect of cigarette smoking on the survival of free vascularized and pedicled epigastric flaps in the rat. Plast Reconstr Surg 1996; 97: 86-96.

- 14) CHEN HC, COSKUNFIRAT OK, OZKAN O, MARDINI S, CIGNA E, SALGADO CJ, SPANIO S. Guidelines for the optimization of microsurgery in atherosclerotic patients. Microsurgery 2006; 26: 356-362.
- 15) COURI CE, DA SILVA GA, MARTINEZ JA, PEREIRA FDE A, DE PAULA FJ. Mönckeberg's sclerosis - is the artery the only target of calcification? BMC Cardiovasc Disord 2005; 5: 34.
- 16) MICHELETTI RG, FISHBEIN GA, CURRIER JS, FISHBEIN MC. Mönckeberg sclerosis revisited: a clarification of the histologic definition of Mönckeberg sclerosis. Arch Pathol Lab Med 2008; 132: 43-47.
- 17) REID SK, PAGAN-MARIN HR, MENZOIAN JO, WOODSON J, YUCEL EK. Contrast-enhanced moving-table MR angiography: prospective comparison to catheter arteriography for treatment planning in peripheral arterial occlusive disease. J Vasc Interv Radiol 2001; 12: 45-53.
- 18) LOEWE C, SCHODER M, RAND T, HOFFMANN U, SAILER J, KOS T, LAMMER J, THURNHER S. Peripheral vascular occlusive disease: evaluation with contrast-enhanced moving-bed MR angiography versus digital subtraction angiography in 106 patients. AJR 2002; 179: 1013-1021.
- 19) ADRIAENSEN ME, KOCK MC, STUNEN T, VAN SAMBEEK MR, VAN URK H, PATTYNAMA PM, MYRIAM HUNINK MG. Peripheral arterial disease: therapeutic confidence of CT versus digital subtraction angiography and effects on additional imaging recommendations. Radiology 2004; 233: 385-391.
- 20) OUWENDUK R, DE VRIES M, PATTYNAMA PM, VAN SAMBEEK MR, DE HAAN MW, STUNEN T, VAN ENGELSHOVEN JM, HUNINK MG. Imaging peripheral arterial disease: a randomized controlled trial comparing contrast-enhanced MR angiography and multi-detector row CT angiography. Radiology 2005; 236: 1094-1103.
- RIBUFFO D, ATZENI M, SABA L, MILIA A, GUERRA M, MALLARINI G. Angio computed tomography preoperative evaluation for anterolateral thigh flap harvesting. Ann Plast Surg 2009; 62: 368-371.
- 22) ROZEN WM, RIBUFFO D, ATZENI M, STELLA DL, SABA L, GUERRA M, GRINSELL D, ASHTON MW. Current state of the art in perforator flap imaging with computed tomographic angiography. Surg Radiol Anat 2009; 31: 631-639.
- 23) RIBUFFO D, CHIUMMARIELLO S, CIGNA E, SCUDERI N. Salvage of a free flap after late total thrombosis of the flap and revascularisation. Scand J Plast Reconstr Surg Hand Surg 2004; 38: 50-52.
- 24) SABA L, ATZENI M, ROZEN WM, ALONSO-BURGOS A, BURA R, PIGA M, RIBUFFO D. Non-invasive vascular imaging in perforator flap surgery. Acta Radiol 2013; 54: 89-98.
- 25) SABA L, ATZENI M, RIBUFFO D, MALLARINI G, SURI JS. Analysis of deep inferior epigastic perforator (DIEP) arteries using MDCTA: comparison between 2 post-processing techniques. Eur J Radiol 2012; 81: 1828-1833.
- 26) PARK S, HAN SH, LEE TJ. Algorithm for recipient vessel selection in free tissue transfer to the lower

- extremity. Plast Reconstr Surg 1999; 103: 1937-1948.
- MULHOLLAND S, BOYD JB, McCABE S, GULLANE P, ROT-STEIN L, BROWN D, YOO J. Recipient vessels in head and neck microsurgery: radiation effect and vessel access. Plast Reconstr Surg 1993; 92: 628-632.
- ARNEZ ZM. Immediate reconstruction of the lower extremity-an update. Clin Plast Surg 1991; 18: 449-457.
- 29) ISENBERG JS, SHERMAN R. Zone of injury: a valid concept in microvascular reconstruction of the traumatized lower limb? Ann Plast Surg 1996; 36: 270-272.
- MAT SAAD AZ. Simple irrigation technique for microvascular surgery. Plast Reconstr Surg 2007; 119: 2342-2343.
- D'ARPA S, CORDOVA A, MOSCHELLA F. Pharmacological thrombolysis: One more weapon for free-flap salvage. Microsurgery 2005; 25: 477-480.
- 32) KHOURI RK, COOLEY BC, KUNSELMAN AR, LANDIS JR, YERAMIAN P, INGRAM D, NATARAJAN N, BENES CO, WALLEMARK C. A prospective study of microvascular free-flap surgery and outcome. Plast Reconstr Surg 1998; 102: 711-721.
- 33) RITTER EF, CRONAN JC, RUDNER AM, SERAFIN D, KLITZ-MAN B. Improved microsurgical anastomotic patency with low molecular weight heparin. J Reconstr Microsurg 1998; 14: 331-336.
- 34) KHOURI RK, SHERMAN R, BUNCKE HJ JR, FELLER AM, HOVIUS S, BENES CO, INGRAM DM, NATARAJAN NN, SHERMAN JW, YERAMIAN PD, COOLEY BC. A phase II trial of intraluminal irrigation with recombinant human tissue factor pathway inhibitor to prevent thrombosis in free flap surgery. Plast Reconstr Surg 2001; 107: 408-415.
- 35) XIPOLEAS G, LEVINE E, SILVER L, KOCH MR, TAUB PJ. A Survey of microvascular protocols for lower extremity free tissue transfer I: perioperative anticoagulation. Ann Plast Surg 2007; 59: 311-315.
- 36) OZKAN O, OZGENTAS HE. Open guide suture technique for safe microvascular anastomosis. Ann Plast Surg 2005; 55: 289-291.
- 37) SERLETTI JM, DEUBER MA, GUIDERA PM, HERRERA HR, READING G, HURWITZ SR, JONES JA, OURIEL K, GREEN RM. Atherosclerosis of the lower extremity and free-tissue reconstruction for limb salvage. Plast Reconstr Surg 1995; 96: 1136-1144.
- 38) KHOURI RK, COOLEY BC, KUNSELMAN AR, LANDIS JR, YERAMIAN P, INGRAM D, NATARAJAN N, BENES CO, WALLEMARK C. A prospective study of microvascular free-flap surgery and outcome. Plast Reconstr Surg 1998; 102: 711-721.
- ALBERTENGO JB, RODRIGUEZ A, BUNCKE HJ, HALL EJ. A comparative study of flap survival rates in end-toend and end-to-side microvascular anastomosis. Plast Reconstr Surg 1981; 67: 194-199.
- 40) SAMAHA FJ, OLIVA A, BUNCKE GM, BUNCKE HJ, SIKO PP. A clinical study of end-to-end versus end-to-

- side techniques for microvascular anastomosis. Plast Reconstr Surg 1997; 99: 1109-1111.
- CONRAD MH, ADAMS WP JR. Pharmacologic optimization of microsurgery in the new millennium. Plast Reconstr Surg 2001; 108: 2088-2096.
- 42) JOHNSON PC, BARKER JH. Thrombosis and antithrombotic therapy in microvascular surgery. Clin Plast Surg 1992; 19: 799-807.
- 43) XIPOLEAS G, LEVINE E, MD, SILVER L, KOCH RM, TAUB PJ. A survey of microvascular protocols for lower extremity free tissue transfer ii postoperative care. Ann Plast Surg 2008; 61: 280-284.
- 44) TSUCHIDA Y. Age-related changes in skin blood flow at four anatomic sites of the body in males studied by Xenon-133. Plast Reconstr Surg 1990; 85: 556-560.
- 45) THOMPSON JG, KERRIGAN CL. Hydrogen clearance: assessment of technique for measurement of

- skin-flap blood flow in pigs. Plast Reconstr Surg 1991; 88: 657-663.
- 46) CASANOVA R, IRIBARREN O, GROTTING JC, VASCONEZ LO. Clinical evaluation of flap viability with a dermal surface fluorometer. Ann Plast Surg 1988; 20: 112-116.
- 47) KAUFMAN T, GRANICK MS, HURWITZ DJ, KLAIN M. Is experimental muscle flap temperature a reliable indicator of its viability? Ann Plast Surg 1987; 19: 34-41.
- 48) GENDEN EM, RINALDO A, SUÁREZ C, WEI WI, BRADLEY PJ, FERLITO A. Complications of free flap transfers for head and neck reconstruction following cancer resection. Oral Oncol 2004; 40: 979-984.
- CHO BC, SHIN DP, BYUN JS, PARK JW, BAIK BS. Monitoring flap for buried free tissue transfer: its importance and reliability. Plast Reconstr Surg 2002; 110: 1249-1258.