1. Patho-physiology of pressure ulcers

Pressure ulcers are reflecting patients' systemic health; physical, nutritional, social and psychological status. The complex pathophysiology suggests that several step-ladder of the evolution is required. First, the sustained pressure force or shear force continued over soft tissue in between body mass, bony process and surface. Capillary vessel flow reduced, then blood vessel and lymphatic vessel occlusion and capillary thrombosis followed. Tissues are ischemic in this condition and reactively capillary permeability increased and the fluid is collected in the third space (extra-vascular space). Edematous tissues may result in necrosis, which is irreversible. Once tissue developed necrosis, precisely enough debridement is considered. Surgical intervention may start when to evaluate the necrosis of tissue and how to remove effectively from the healthy surrounding tissue (Table 1).

2. Importance of debridement-indications and contra-indications

Pressure ulcer can speedily and correctly be treated by surgical intervention. Surgical debridement is the mainstay in facilitating chronic pressure ulcer wounds to healing phase if properly applied. In preparation of wound beds, surgical debridement contributes to removal of necrosis, removal or reduction of infectious bacterial load or biofilms, corrupt matrix or senescent cells. Currently, the most commonly used grading scale is that developed by the National Pressure Ulcer Advisory Panel (NPUAP)(Table

2). Originally, the scale consisted of four stages, based on visual examination of the ulcer. The scale was modified in 2007 to include two other stages, for deep-tissue injury and unstageable ulcers (Table 2). Surgery is implicated in stage II, III and IV. In stage II, the partial damage to the skin even though most of the cases wounds in this stage are often reversible as a natural course observation. In stage III, the wounds depth reaching the fascia and ischemic-irreversible, slough and necrotized tissues are recommended to perform surgical debridement and determined and cut open for the surrounding and peripheral spread undermining and tracts. Usually stage III lesions over the heel, malleolus, or patella/knee that have developed as the result of immobilization, splinting or bracing are not as deep as lesions found over the hip or gluteal region.

Some pressure ulcers that are unstageable and require debridement, which may result in a stage IV ulcer. These ulcers have exposed bone, tendon, and/or muscle in the wound bed, which often is covered by eschar (dried necrosis) tissue at the base of the wound. Removal of the overlying eschar reveals the exposed underlying tissue and the presence of undermining or tunneling tracts distally and underneath the intact skin from the wound edge. The patient with a stage IV ulcer is at risk of developing osteomyelitis, because the wounds are penetrated to the bone. Stage IV ulcers do not go through a progression of healing via the previous three stages until resolution. In stage IV, "reverse staging" to the better stage is not possible and is an inaccurate method of describing improvement or deterioration and of determining treatment. Healing occurs via contraction and scar formation, however, adequate-enough debridement in width

and in depth is ideal for faster healing.

In the modified NPUAP staging system was included unstageable areas as well as injuries that fall under the category of pressure-induced necrosis of muscle with intact skin.

As muscle tissue is more sensitive to ischemia than an overlying skin is, compression between surface and bony prominence results in earlier damage to muscle tissue than to local skin as a result of occluded blood and lymphatic vessels. Indications of deep tissue injury include an area that appears maroon or purple in color and a blood-filled blister in an area of intact skin. The area may initially present with warm, painful skin that may be firm or boggy compared with the surrounding tissue. These deep tissue injuries can evolve rapidly from an apparently minor skin lesion to one that involves exposure of deeper layers. This evolution can progress through additional layers of skin despite of optimal treatment. Surgical exploration and debridement is useful for both diagnosis of the level of deep tissue injury and for decompression and removal of necrotized tissue.

Unstageable ulcers are characterized by a deep ulcer or by multi-layer tissue loss, and they also contain a large amount of slough or eschar tissue in the wound bed. Adequate debridement is necessary for revealing characteristics of ulceration.

When undergoing the surgical debridement and removal of eschar, slough, necrosis, care should be taken to avoid the massive bleeding from the intact tissue and vessels. All procedures are performed as atraumatic as possible. Hemostasis with electro-cautery, ligation and compression are prepared to all the cases in advance. Surgically-obtained

specimens are sometimes used for quantitative tissue culture assessment.

In patients with coagulopathy, medication of anti-coagulants and bleeding-tendency, it is paid a special attention prior to the surgical procedures to control and to normalize the systemic condition. If the local blood supply or tissue perfusion is insufficient and anti-bacterial coverage for current and potential septic status is lacking, surgical debridement is not recommended.

3. Choice of the surgical debridement

Wound bed preparation by sharp and mechanical debridement with surgical instruments is most fundamental method for adequate wound healing management. It is able to reduce most selectively and effectively a bio-burden of a wound. To eliminate of necrotic tissue, which behaves as a substrate for proliferating bacteria that strives for the same nutrients and oxygen molecules essential for wound healing, is crucial for the promotion of the normal wound-healing process of tissue. If the border of the normal healthy and devitalized skin is not determined clearly, tangential excision, starting at the center of the necrotic skin, should be considered until scattered bleeding observed in the dermis. Bleeding is less indicative for subcutaneous tissue debridement, because fat tissue is poorer in vascularity than skin is. Debridement until shimmering yellowish fat tissue level should be performed. Hemostasis is usually achieved by clamping or

compression. Scattered bleeding is well controlled with electro-cautery. If bleeding from greater-diameter vessels, ligation with monofilament suture is attempted.

Non-vascularized fascia should be removed with a special caution to the neurovascular bundles in the superficial vicinity. Muscle, tendon, cartilage and bone in Stage IV can be resected when apparent blood supply is not observed. In case of deep tissue injury, sharp penetration to the muscle and deeper tissue level is very helpful for determining the extension of the wounds.

Surgical equipment composes of scalpel blades, pickups, electro-cautery, scissors, curettes, rongeurs, Harmonic Scalpel, Cavitron Ultrasonic Surgical Aspirator (CUSA®), waterjet (hydrojet) system (Versajet), elevators, chisels, osteotomes, saws, rasps, and burrs and so on. Simple incisions and minor resections can be performed at the bedside if the methods of hemostasis are ready, however, deeper and wide surgical debridement is planned at the operation ward where appropriate lighting, anesthesia, irrigation, suction systems and man-power are provided.

Most frequently used instruments are scalpel blades and they should be exchanged to new ones when the blade edges become dull. There are two types of scalpel blades. One is the round-tip and the other is pointed-tip. Both No. 10 and No. 15 blades contain the round-tip edges. The No. 10 scalpel is one of the more traditional blade shapes and is used generally for making small incisions in skin and muscle, while The No.15 blade has a small curved cutting edge and is the most popular blade shape ideal for making short and precise incisions for deeper tissues. No. 11 scalpel blade is an elongated

triangular pointed-tip edge blade sharpened along the hypotenuse edge and with a strong pointed tip making it ideal for stab incisions. With such characteristics, it is also used for screening and evaluating by stabbing the deeper tissues of the fascia and muscle to evaluate the deep tissue injury. For this purpose, pointed-tip edge scalpel blade is more frequently used to try to open through a small incision.

Harmonic Scalpel, utilized ultrasonic energy to enable hemostatic cutting and coagulation of tissue, enable a surgeon to incise tissue when hemorrhage control and minimal thermal injury to surrounding tissue are required. Cavitron Ultrasonic Surgical Aspirator (CUSA®) transmits a 23 KHz ultrasonic vibration to the tip of the hand-piece and enable the target tissue disruption and cool saline water irrigate surrounding tissue and aspirate the resected tissue. This systems leave elastic bold vessel, biliary, tact, fascia and nerves but disrupt parenchymal, fat and tumor tissue selectively, In neuro-, haptic- and oncologic surgeries, it is often used. CUSA® is useful for debridement of deep and wide wounds near bold vessels and nerves. Versajet hydrosurgey system contains a razor-thin saline jet for surgical debridement. This system brings about reduction of bacterial burden in the wound, preservation of viable tissue and removal of unwelcome necrosis and debris. The hand piece of the system can tangentially move over the soft tissue surface and prepare wound bed.

Hard tissues such as bone, cartilage and calcified tissue are removed by curettes, rongeurs, elevators, chisels, osteotomes, saws, rasps, and burrs. The size, hardness, tissues-attached is considered in selection.

Surgical debridement is the most essential procedure for both treatment and diagnosis in the presence of osteomyelitis. Primary closure or delayed primary closure by reconstructive procedures or wound closure by secondary intention is followed post-debridement.

4. Choice and indication of coverage

A: Negative Pressure Wound Therapy

Even though it is optimal to cover right after surgical debridement by some mean of reconstructive procedure, however, sometimes affiliated factors such as systemic conditions of the patients, extensiveness of the wounds and unsure bacterial control of wound bed will lead to wound closure by secondary intention. There are many diverse efforts spent to develop for this purpose and negative pressure wound therapy (NPWT) is one of the most powerful and effective methods in post-surgical wound closure, management or together with skin grafting or artificial dermis (1)

Prospective clinical study with severe pressure ulcer, over 80% are stage IV, patients with infection can be safely and successfully undergone surgical debridement and managed with vacuum-assisted closure (VAC) therapy post-surgically (2). VAC®, one of NPWTs, is useful for pressure ulcer with osteomyelitis 3 out of 13 cases in 6-weeek observation period in comparison to treatment with three gel products, which demonstrated no improvement by MRI or bone biopsy (3). NPWT becomes an integral

part of wound treatment by improving wound tissue perfusion, increasing granulation tissue, decreasing bacterial counts, reducing excessive wound fluid, enhancing physiologic cellular pathways.

In a randomized, prospective study of surgical debrided-pressure ulcer wounds, comparing with wet-to-dry/wet-to-wet gauze soaked with Ringer's solution, NPWT is superior in reducing treatment cost and improving comfort of less frequency of dressing change (4). NPWT is used for adjunctive procedure following skin grafting and applying of artificial dermis. In small to medium-sized wounds exposing bone, joint and tendon, autologous mesh dermal grafting followed by split-skin grafting in 2 weeks led to successful wound closure (5)(Figure 1). In complex combat-related severe soft tissue loss with exposure of tendon and bone, pre-operative VAC, right after surgical debridement followed single or multiple artificial dermis and VAC and secondary skin grafting resulted in more than 80% wound coverage (6).

B: Closure by reconstructive surgery

Stage III and stage IV pressure ulcers may require some kind of reconstructive procedures for wound closure if not intended secondary wound healing, which takes longer time and results in higher risk such as infection during clinical course, especially stage IV of exposed bone. There are numerous reconstructive procedures reported. Special attentions and considerations should be paid to each reconstructive procedure, anatomical location of the ulcer.

In case of stage IV and osteomyelitis are concerned, preoperative magnetic resonance imaging diagnosis is helpful. The failure of clarification and proper management of osteomyelitis leads to high rate of recurrence or worsening of the symptom. The principle of management of osteomyelitis lies on total resection of non-viable bone and antibiotic therapy proved by bone biopsy (7). Patients with osteomyelitis diagnosed by MRI demonstrated similar ulcer recurrences to patients with osteomyelitis diagnosed by bone culture (8). In this report, the patients with a diagnostic preoperative MRI did not differ significantly in rates of antibiotic administration, ostectomy, dehiscence, revision, or infection.

1) Skin grafting

Skin grafting is the simplest method for wound closure; however, skin grafting is not ideal for weight-bearing area. Thus, only small population with non-weight bearing area of stage III and when systemic conditions requiring earliest wound closure to avoid exudates and insensible water loss are candidate for this procedure (Figure 2).

Recently, a combined use of skin grafting and negative pressure wound therapy demonstrates Bolster and splinting effect in skin grafting to the forearm free flap donor (9) and reliable split-thickness skin grafting dressing for lower limb defects (10). Where higher pressure and shear pressure are considered, alternative procedures such as flap reconstruction is desired.

2) Flaps

There are many flaps are proposed for pressure ulcer wound closure. The pattern of blood perfusion, tissue and location of the flap donors are varied and anatomical and physiologic issues are taken into account.

i) Flap type

Local skin flap such as V-Y advancement flap, rotation flap, Limberg flap can be used for smaller-sized defects. Recent knowledge of vascular anatomy in skin and subcutaneous areas enables surgeons to use perforator flap antero-lateral perforator to "freestyle" perforator flaps (11)(12)(Figure 3). Most commonly used composite flaps are musculocutaneous and fasciocutaneous flaps in pressure ulcer reconstruction. In paraplegic and tetraplegic patients, musculocutaneous flaps are often used, because loss of muscle is less severe. Muscle volume may fill in the deep wound defect post-surgical debridement, eliminating dead space and muscle of musculocutaneous flap may serve as a blood supplier of overlying soft tissue and skin, a cushion of pressure-relieving, provider of the potential infection control by abundant blood flow. However, muscle is less tolerant to ischemic condition.

Fascia is better in resistance of pressure and mechanical stress than muscle and thus greatly applied to the higher pressure and shear stresses wounds (13). Clinical study indicates that the musculocutaneous flaps are not superior to fasciocutaneous flaps in the reconstruction of pressure ulcers. Both fasciocutaneous flaps and musculocutaneous

flaps are usable but only extremely large defects justify the use of muscle, usually a fasciocutaneous flap is sufficient to cover the average size lesions. These results question the long-standing dogma that muscle is needed in the repair of pressure ulcers (14).

In selective cases, free flap transfer is applied when the defect is too large to cover by the local flap and free flap cases seem greater percentage in diabetic, incontinence and paraplegia (15).

ii) Location

Sacral ulcers

Sacral ulcers develop in patients who prolonged to rest on bed. Sacral pressure ulcer wounds require removal of the bursa, with dye staining inside of lumen. When the bone is necrotic, sacrectomy by osteotome and/or rongeur is recommended to use. After surgical debridement is finished, musculocutaneous using gluteus maximus muscle, fasciocutaneous, cutaneous or perforator flap is elevated by skin design of rotational, rotation-advancement or V-Y advancement flap. When the patient is sensate and in an intact hip function, gluteus maximus muscle should be preserved. Or part of gluteus maximus muscle is used as a "split" musculocutaneous flap with rich blood supply from para-sacral perforators and maintains the majority of the deep muscle and hip joint function (16).

Perforator flaps, of which blood vessels reach up to the skin by perforating through

muscle and /or fascia underneath various para-sacral areas is beneficial for lower recurrence rate of 2.9% in 32 cases and durable for a mean follow-up for 13 months (17).

Gluteus fasciocutaneous rotation-advancement flap with V-Y closure, which adapts both merit of rotational and V-Y advancement with minimal skin incision, is also effective procedure for coverage of sacral defects (13) and for larger defects, modified bilateral gluteal V-Y advancement fasciocutaneous flap may be used (18).

Ischial ulcers

Ischial ulcers are characteristic of a small skin defect and a large cavity or bursa formation underneath. An ischial pressure ulcer is caused from sitting and paraplegic patients with wheelchairs may have remarkable pressure and shear forces during sitting. Until complete wound healing, bed-rest is required. Ischial ulcers are one of multivariate predictors of recurrence and multivariate predictors of late recurrence as well as previous same-site failure, poor diabetic control or age younger than 45 years (19). Ischial flap reconstructions is often interfered by movement over the ischium, pressure or shear exerting over ischium during sitting and fails to protect adequately. Excursion of soft tissues attached to the patient trunk or pelvis is great according to the pelvis/thigh positioning, thus coverage of ischial bony prominence is easily detached. This is one of the reasons of late recurrence.

Musculocutaneous, fasciocutaneous, perforator-based flaps are employed. Inferior

gluteus maximus musculocutaneous flap is able to provide enough blood supply and issue volume to cover deep ulcers but most of perforators from the inferior gluteal artery is scarified by elevating this flap and thus results in division of gluteus maximus muscle, which is contra-indicated for ambulatory patients. Tensor Fascia Lata (TFL) musculocutaneous flap can be an innervated flap for patients with sensory at third lumber level. With TFL musculocutaneous flap, both ischial and trochanteric ulcers can be covered simultaneously. The pedicle of TFL is consistent but relatively short and tissue of the proximal area is greater than distal end. TFL can combine vastus lateralis Musculocutaneous flap. Gracilis musculocutaneous flap provides simple, strong and effective in relatively small- to medium-sized defects. Since gracilis muscle composes a large-caliber vessel even though muscle belly may be atrophied especially in a paraplegic patient (20). Posteromedial fasciocutaneous flap is effective both in primary and recurrent ischial ulcer closures (21) and long-term follow-up outcome at mean of 62 months, by laterally-based posterior-thigh fasciocutaneous flap demonstrated complete primary wound healing for all of 12 cases and 2 of 12 cases demonstrated stage II ischial ulcer recurrence at 24 and 27 months, respectively (22).

Inferior gluteal artery perforator (IGAP) flap demonstrated clinically almost 80% (18 of 23 cases) without recurrence averagely 25 months' post-operative follow-ups (23). For recurrent cases, combined gracilis muscle flap and V-Y profunda femoris artery perforator-base flap can provide enough bulk in the dead space and mechanical resistance (24). Medial planter flap, which is more resistant to shear stress due to its

anatomical characteristics, is also used for recurrent ulcers for paraplegic and active in wheel-chairs (25)(Figure 4).

Trochanteric ulcers

Although less frequently in compared to sacral, ischial ulcers, once the pressure ulcer is developed in trochanteric region, it is usually larger undermining and deeper tissues involved. The trochanteric bone is well mobile and thus the stabilization after reconstruction of the surface of the trochanteric bone is not easily achieved. Trochanteric pressure sores develop in patients who lie in the lateral position, especially in those with significant flexion contracture (26). Successful treatment requires a multidisciplinary approach and good surgical planning. Debridement should reach deep enough affected tissue, sometimes to bony prominences with smoothing the surface. Since first introduced, the TFL flap has become a standard approach for the management of trochanteric defects (27). However, the disadvantages of flap tip necrosis and dog-ear deformity from its original design led surgeons to look for new designs for this flap. Some modifications were proposed, such as the bilobed flap (28), the advancement V-Y flap (29) and the retroposition V-Y flap (30)(Figure 5). Despite these successful alternatives, the problems of prolonged operative time and unaesthetic scars remained. Recurrent rates of up to 80% have been observed with the treatment of trochanteric pressure sores using musculocutaneous flaps based on the TFL. The primary consideration in the surgical treatment of trochanteric pressure ulcers is the

need to fill skin and soft tissue losses, and coverage of the greater trochanter with a durable, well-perfused musculocutaneous flap. The pedicled anterolateral thigh (ALT) musculocutaneous flap is suitable for this purpose. 21 consecutive ALT musculocutaneous flap, mean follow-up of 13 months, demonstrated successful wound closures without recurrence (31).

In two cases of using superficial gluteal artery, "free-style" local perforator flaps succeeded in closure of the wounds sized 12×20 cm and 16×30 cm with follow-ups of 12 months, 14 months, respectively (12).

Heel ulcers

Posterior heel is common area of pressure ulcers among bed-bound patients or immobile patients. Wound coverage to exposed tendon and/or underlying calcaneal bone is difficult because the local blood supply and tissue perfusion are deprived. Durable, well-perfused and proper-sized flaps are needed. A lateral calcaneal artery skin flap is widely used for coverage of the tendon and calcaneus area and modification by an island flap diminishes the kinks of the pedicles (32). V-Y modification of a lateral calcaneal artery flap takes advantage of no need of skin grafting in donor site (33).

Medial plantar artery flap is useful for reinnervation of the heel for patients who maintain the medical plantar nerve. In 51 flaps used of 48 patients demonstrated 98 % flap survival (34). Reverse flow sural artery-based adipofascial, adipofaciocutaneous, flaps are used for heel ulcers. Reverse sural artery flap is effective in high-risk patients

such as diabetic neuropathy, critically ischemic limb, end-stage of renal disease, nonetheless the systemic condition, 10 of 15 reconstructions were successful (35).

5. Post-operative management

Adequate operative and post-operative management scheme is fundamental for successful results. Conditioning of the systemic nutrition status, normalizing anemic, hypo-albuminemic and abnormal blood cholesterol levels are primarily important. Wound drainage in the reconstructed areas to prevent post-operative seroma, hematoma, surgical site infection (SSI). In a prospective randomized clinical trial of comparison between a closed-suction drain and a Penrose drain after a colectomy revealed no significant difference in SSI rate but a closed-suction management is useful in cost- and labor- savings and reduction of medical wastes (36).

Post-operative reconstruction, care should be paid to the reconstructed flap at least for several weeks by repositioning every 2 hours for patients with para- or quadriplegias. Tissue viability is well preserved by pressure-relieving bedding. Multicenter, randomized controlled clinical trials including surgical patients, treated with an alternative pressure air mattress developed fewer heel ulcers and less worsening from stage I to later stage compared to a visco-elastic foam mattress (37).

In a severe case of extensive and multiple pressure ulcers, it may be useful for applying air-fluidized bed, which provides ultimate weightlessness in the hospital setting, will function pressure-relief for several weeks post-operatively (38).

6. Preparing wound bed and use of bFGF

The recombinant form of glycoprotein cytokines are highly paid attention. Among those cytokines, basic fibroblast growth factor (bFGF) is because it promotes wound bed preparation by mesenchymal cell proliferation for collagen synthesis, mitogenic and chemoattractant for endothelial cells and induction of neovascularization for increase of granulation, and mitogenic to keratinocytes (39)(40). Randomized, placebo-control, prospective recombinant bFGF treatment for stage III and IV pressure ulcers of 50 wounds ranging from 10 to 200 cm^3 with mechanical debridement when necessary 24 hours prior to initial treatment demonstrated greater healing effects and more patients were over 70% wound closure (39). In burn ulcer treatment, sharp debridement, human recombinant bFGF application to the wound after surgical debridement with mesh split-thickness skin grafting and continued bFGF application over mesh skin grafts resulted in faster skin grafting healing and softer and durable scar formation (41). In meantime of definitive reconstructive surgery, it is important to prepare better wound beds and use of human recombinant bFGF may be a candidate for this purpose.

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