



Review Article

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VARIABLES INFLUENCING THE BONE HEALING PROCESS: AN AYURVEDIC REVIEW WITH MODERN INTERPRETATION

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ABSTRACT

Fracture generally affects the physical, psychological, emotional, financial and social aspects of a person's life. The ever increasing incidences, disability and agony associated with it necessitate its early and effective management. Fracture healing is by the regeneration of the bony tissues. This healing process can be altered by various internal and external factors. Today, knowledge of a wide range of factors influencing fracture- healing is available in the modern medicine. In Ayurvedic literature also, a cascade of factors influencing the fracture healing has been described. But a systematic compilation of these factors with the definitive modern scientific basis is lacking. Majority of the factors described in the texts of modern system simulate with those described in Ayurveda. By a keen understanding of the influences exerted by these factors, a rational modification can be done in the fracture management strategies. In Ayurveda, consideration has been given to the factors which influence the healing viz. Prakriti, type of injury, tissues involved, associated injuries, concomitant diseases, effect of season, treatment methods etc. A thorough knowledge of all such factors along with their practical applicability is necessary for a successful management. This paper reviews Ayurvedic literature concerning the variables which can alter the healing of fractures with possible modern interpretation.

KEY WORDS: Fracture, Healing, Variables, Ayurveda, Influence.

INTRODUCTION

The incidences of fractures are constantly increasing day by day; affecting all the age groups particularly in young. This is resulting into the greater physical, psychological and financial loss to the patients and their families. As the aged population increasing, fragility fractures, such as those of the neck of femur are also becoming more common and a higher percentage of fractures may have difficulties in healing¹. Much of the national resources are being driven out by the trauma victims. Owing to the great deal of disability and suffering associated with the injuries, a prompt and effective management is required. Management of a fracture requires a rational and holistic approach, taking into consideration the various factors influencing the healing process. By a keen understanding of the influences exerted by these factors, modifications can be done in the fracture management strategies. Modern science has described a wide range of the variables which can alter the healing process. In Ayurveda also, due consideration has been given to the factors which influence the healing viz. Prakriti, type of injury, tissues involved, associated injuries, concomitant diseases, effect of season, treatment methods etc. But a systematic compilation of these factors with the definitive modern scientific basis is lacking. A thorough knowledge of all such factors along with their practical applicability is necessary for a successful management.

Fracture healing is a complex, unique physiological process of repair in which bone heals for the purpose of transferring mechanical loads². The majority of fractures unite by secondary bone healing. This progresses in five stages, as originally described by McKibbin³ namely hematoma formation,

inflammation³, formation of soft and then hard callus and finally remodeling. Different agents or pathological processes may affect all of these stages or only one. Primary bone healing occurs when there is rigid internal fixation. This consists of cutting cones (tunneling osteoclasts followed by osteoblasts forming new bone) which progress across the fracture site directly in a similar way to normal bone remodeling. Both forms of healing are brought about by a series of distinct cellular responses which are under the control of specific paracrine and autocrine intercellular signalling pathways and can be interrupted by different factors.

Variables influencing fracture healing

Occasionally delayed unions or non-unions occur without apparent cause, but in many instances injury, patient and treatment variables that adversely influenced the fracture healing can be identified. These variables include severe soft tissue damage (open and high energy closed fractures), infection, segmental fractures, pathological fractures, soft tissue interposition, poor local blood supply, systemic diseases, malnutrition, vitamin D deficiency, corticosteroid use, poor mechanical fixation, and iatrogenic interference with healing⁴. Permeation through Ayurvedic literature related to Bhagna (skeletal injuries) reveals that numerous such factors have been described in it. However, the methodology of description is different and discrete. We do not find these at one place or in one chapter. Few of such factors have been mentioned in Nidana Sthana of Sushruta Samhita⁵ and others are in Chikitsa Sthana⁶. In other classical texts like Vagbhata⁷, Yogaratnakara, Sharangdhara⁸ and Bhava Prakasha⁹ also we find the references of such variables. These factors can be grouped as:

- Injury Variables
- Patient Variables
- Tissue Variables
- Treatment Variables
- Other variables

Injury variables

Type of fracture: Morphology of a fracture is an indicator of the mechanism & magnitude of injury. It also gives a clue to the possible prognosis and outcome of the treatment. Forces with different kinds of magnitude and directions acting upon the body or bone produce different types of fractures. A fracture or joint injury is not merely the bone or joint injury but is a complex mechanism which includes the injuries to adjoining soft tissue structures as well. Extensive damage to the soft tissues results into decreased number of mesenchymal cells and disrupted local vascularity, more tissue necrosis; all factors hampering the healing of tissues¹⁰. In Ayurveda some types of Kandabhagna (fractures) are considered as Krichha Sadhya (Difficult to treat) viz. Churnita (comminuted fracture), Chhina (Marginal fractures with severe displacement), Ati patit (Complete displaced fracture), Majja-anugata (Impacted fracture) and Sandhi-upgata (Intra-articular or fracture line extending to the joint)¹¹

Churnit Bhagna¹² (comminuted fracture) is generally the result of high energy trauma that leads to extensive tissue damage and loss or decreased blood supply. However, some patients with osteopenia or osteoporosis may sustain such type of fractures with low energy trauma. Displacement of fragments and poor blood supply retard the healing of such fractures. Such fractures pose difficulty in reduction and immobilization¹³.

Chhina (marginal fractures with severe displacement), Ati patit¹⁴ (Complete and displaced fracture), are the injuries where fracture fragments seem to be displaced or distracted. These fractures are likely to land in delayed union or non-union until they are properly reduced and immobilized.

Majja-anugata Bhagna¹⁵ are generally accepted as impacted fractures. Impacted fractures occur in various regions of different bones. Most of the times, these pose little difficulty in healing because they are stable. But if they are badly impacted with rotation or angulation can result into severe deformity, if not properly reduced. Sometimes splintered fragments get rotated and impacted within the medullary canal and may result into delayed union or non unions until unless they are surgically tackled. Femoral neck fractures are generally impacted fractures and famous for non union due to the deficient blood supply to the proximal fragment.

Sandhi-upgata¹⁶ (intra-articular or fracture extending to the joint) cause vanishing of fracture hematoma, movements at the joint and synovitis. These exert negative effects on healing. Also, there is possibility of early secondary osteoarthritis of the joints involved.

Joint motion or loading may cause movements of the fragments resulting into challenging treatment problems. Most intra-articular fractures heal, but if the alignment and congruity of the joint surface is not restored, the joint surface will become incongruous and the joint may be unstable resulting into secondary osteoarthritis¹⁷.

Associated complications: A variety of complications can originate with the skeletal trauma. These complications may be local or generalized and can be due to fracture itself, treatment,

surgery or anesthesia. Such associated complications pose difficulty in fracture healing. Sushruta in chikitsa Sthana 3rd chapter has quoted that skeletal injuries of Updravyervajushtasya (associated with complications) are difficult to heal¹⁸. Dalhana while commenting on this has mentioned few such complications like jwara (fever), adhmaan (abdominal distension), mootrapurishsanga (anurea or oligurea and absolute constipation) etc.¹⁹. Such co-morbidities or complications can occur in polytrauma patients, crush syndrome, shock, local or systemic infection or paralytic ileus. Due to these associated problems, management and ultimately healing of the fractures is difficult.

Patient variables

Age: Patient's age significantly influences the bone healing²⁰. According to Ayurveda, fractures occurring in young age heal earlier than middle and old ages²¹. Infants have the most rapid rate of fracture healing. Rate of healing declines with the advancing age. Multiple factors contribute to age-related changes in fracture healing, including decreased number and function of stem cells, decreased chondrogenic potential of the periosteum, changes in the local signaling of the milieu at the fracture site, and impaired vascularisation^{22,23}. Cells of young patient may differentiate rapidly from the mesenchymal pool. In Vridhha-avastha (old age), all Dhatus (body tissues), energy and vitality decrease and Vata Dosha (a body humor) is aggravated in general. Due to the poor availability of healing material and age related Vata Vridhhi, fracture healing may be delayed.

In Nidana Sthana, Sushruta has indicated that fractures of children are difficult to heal and manage²⁴. This statement is not the contradiction of the statement that fractures in children heal rapidly²⁵ because, in Balaavastha (children) although the healing process is fast owing to a larger pool of mesenchymal cells available for healing; yet due to the un-co-operative nature of the children, delicacy, inability to tolerate the cumbersome treatment; fractures of children pose difficulty in management.

Nutritional Status: If the patient is 'Krisha' (emaciated – malnourished) or Alpa-ashino (poor dietary intake), fracture healing gets impaired²⁶. This may be due to the poor status of the body tissues (Dhatus) and the resultant aggravation of Vata Dosha (body humor). Cell migration, proliferation and matrix synthesis necessary to heal a fracture requires substantial energy. Furthermore, to synthesize large volumes of collagens, proteoglycans, and other matrix macromolecules, cells need a steady supply of components of these molecules: proteins and carbohydrates. As a result, the metabolic state of the patient can alter the outcome of injury, and in severely malnourished patients injuries that usually heal rapidly may fail to heal²⁷. Jensen and associate have found that a 42.4% incidence of clinical or subclinical malnutrition in patients undergoing orthopedic surgical procedures²⁸. A study of 490 patients with hip fractures found that 87 of these patients (18%) suffered from malnutrition and that the malnourished patients stayed in the hospital longer, were less likely to recover their pre-fracture level of activity, and were more likely to die within one year of their hip fracture²⁹. These patients also have a poor endurance for the complex and hectic management schedule of technical management of fractures. An experimental study of fracture healing demonstrated that fracture callus does not achieve normal strength in states of dietary deficiency, and that a dietary deficiency of protein reduces fracture callus and energy storage capacity³⁰. For these reasons, injured patients require an assessment of their nutritional status and appropriate treatment, which may include nutritional support³¹.

Lack of self control: Fractures of the patients with poor self control (Anaatmvato) difficult to heal³². Dalhana while commenting on the word Anaatmvato has interpreted this word as Ajitendriya (poor self control) or Apathyasevina (indulging of contra-indicated foods and drinks)³³. Due to lack of self control they may not observe the Do's and Don'ts properly. This may include early discarding of the splints, early excessive movements or weight bearing resulting into non-union, delayed union or even mal-union. Such patient may also indulge incompatible food, alcohol, smoking, excessive and uncontrolled physical activities and least control over their emotions which may have the deleterious effects on the bone healing.

In an experimental study on rat model alcohol consumption has shown the adverse effect on fracture healing³⁴. Similarly cigarette smoking inhibits fracture healing. A study of tibial osteotomy healing in rabbits showed that animals exposed to nicotine healed fractures more slowly and had a higher percentage of non-unions³⁵. Psychological stresses result in to the release of catecholamines which reduce blood flow to the bones and delay the healing³⁶. Incompatible food or imbalanced food ultimately results into poor digestive power, toxin production and malnutrition.

General health and concomitant diseases: Injuries of the persons who are having 'Alpa Dosh Dushti' (minimal disturbance of body humor equilibrium) heal readily³⁷. Indirectly, it can be understood that Bahu Dosh Dushti or disease condition can adversely affect the fracture healing process. Joseph A. et. al. has also mentioned that disease state (local or systemic) can influence fracture healing³⁸. Certain co-morbid conditions either delay the healing process or make the management difficult and ultimately worsen the prognosis. Fractures of the patients of Kshat-Ksheena (Polytrauma patients), Kushtha (Skin diseases) and Shwas Roga (Respiratory distress) have been stated to heal with difficulty³⁹. These conditions either have direct adverse effect on the healing process and also make the technical management difficult.

Kshat-Ksheena (poly trauma) influences the healing process adversely and also makes the technical management difficult. Due to excessive blood loss, soft tissue damage and injuries to vital organs the body demand for nutrition increases and host defense failure occurs⁴⁰. This in the presence of severe nutritional deficiencies makes the patient vulnerable to infections and delays the tissue healing. For the proper fracture healing overlying skin and soft tissue should be healthy, intact with good vascularity particularly for the subcutaneous bones e.g. Tibia and Ulna. Absent or diseased skin is detrimental for fracture healing. Kushtha in Ayurveda pertains to all kinds of skin diseases. Diseased skin poses multitude of problems for the management as well as healing of the fractures. It makes the local technical management difficult and also hampers the fracture healing mechanism due to its own poor status. Vitamin D synthesis may not be adequate through diseased skin which may have adverse impact upon the healing of fractures⁴¹. Furthermore, it may directly infect the fracture hematoma resulting into osteomyelitis.

Shwas Roga includes COPD and Asthma in which there is respiratory distress resulting into poor oxygenation of the tissues. This hypoxic state decreases the partial oxygen tension (PO₂) at the fracture site. Although higher oxygen tensions may generate bone without a cartilage intermediate, it should be noted that this level of oxygen tension is high only relative to other areas of bone. In fact, the overall partial pressure of oxygen found in tissue during bone repair is low when

compared to systemic values. In general, low oxygen tension favors bone healing⁴². But if this oxygen tension falls below the permissible limits may adversely affect the callus formation⁴³. The level of tissue oxygenation may affect fracture repair. Decreasing tissue oxygenation by inducing chronic systemic hypoxia⁴⁴ or by ligating femoral artery delays fracture healing⁴⁵.

Prakriti: Fractures of the patients having Vata dominating Prakriti (Vatatmako) heal with some difficulty^{46, 47}. Prakriti is an important concept of Ayurveda that explains individuality and has role in causation, prevention, diagnosis and treatment of diseases. It expresses unique trait of an individual that is defined by specific and permanent composition of Dosha at conception^{48, 49}. Vatika Prakriti patient, owing to his unstable physical and mental status, has a poor compliance.^{50, 51} Due to these factors patients don't follow the Do's and Don'ts which can hamper the fractures healing process.

Tissue variables

Site and type of bone or joint involved: Bhinna Bhagna (possibly displaced fractures or joint injuries) of Kapala (flat bones or skull bones), Kati (lumbo-sacral region) or Jaghna (iliac or pelvis bones) carry bad prognosis and have been stated as not to be treated⁵². Similarly, the injuries of Lalata (fractures of forehead bones or frontal bones), Stanantara (i.e. in between the breasts possibly the Sternum), Shankha (temporal areas), Prishtha (Back or spine), Moordhani (central part of head or fronto-parietal area) are also not worth treating⁵³. Sushruta has denied treating such injuries⁵⁴. But this should not be considered as the denial of treatment but should be considered as serious injuries with morbidity or mortality. All these sites are Marmas (vital parts). Severely displaced or comminuted fractures or joint injuries at these areas are usually associated with injuries to vital structures like brain, cardio-thoracic region, spinal cord or cauda equine and pelvic organs. It is pertinent to mention that Sushruta has mentioned specific types of injuries (widely displaced fragments or highly comminuted fractures) of these areas which carry bad prognosis and not all types of injuries should be considered as having bad prognosis.

Status of the bone: Bones or joints which are congenitally diseased or deformed (Aadito-durjaata Asthi Sandhi) are likely to have problems in the management or healing of their injuries⁵⁵. Dalhana while commenting on this verse has stated that these are the diseases or deformities which are present since birth⁵⁶. Examples of congenital bone diseases are osteogenesis imperfecta, osteopetrosis, enchondromatosis and achondroplasia. Fractures in patients suffering from these diseases can create lot of problems in terms of treatment, healing and re-fractures. Fractures in osteogenesis imperfecta usually are multiple (due to collagen-I disorders), heal with poor quality of callus with the chances of re-fracture⁵⁷. Osteopetrosis is a condition in which excessive density of bone occurs as a result of abnormal function of osteoclasts⁵⁸. These patient may have multiple fractures and long bones may bow⁵⁹. The onset of callus formation after fracture in Osteopetrosis is variable. Although many studies state that fractures in osteopetrosis heal at a normal rate⁶⁰, others report delayed union and non-union. In a rat model of Osteopetrosis, Marks and Schmidt found delayed fracture healing and remodeling⁶¹. In rickets the outcome of the fracture is good but child is susceptible to recurrent fractures and handling of the patient should be careful to prevent the fractures⁶².

Infection: Clinician should try to prevent infection at the injury site. Once infection settles and suppurates Mamsa (muscles), Sira (veins) and Snayu (ligaments, tendons and fascia) and the treatment and healing of the fracture becomes difficult⁶³. If

infection occurs following a fracture or if the fracture occurs due to infection, many cells are diverted to wall off and eliminate the infection and energy consumption increases. Infection may cause necrosis of normal tissue and thrombosis of blood vessels, thereby retarding or preventing healing. Surgical debridement of infected fracture may cause further tissue damage^{64, 65}.

Antibiotics are frequently prescribed in trauma practice both for the treatment of open fractures as prophylaxis in operated cases or for unrelated conditions such as chest infections. There is a paucity of work in the literature looking specifically at the effect of antibiotics on fracture healing⁶⁶. Three fluoroquinolones have been studied in animal models of fracture repair: ciprofloxacin, levofloxacin and trovofloxacin, and showed that therapeutic doses of each of these diminished healing during the early stages of fracture repair in the rats^{67, 68}. Cell culture studies have shown that the tobramycin, is toxic to osteoblasts in vitro, an observation which is dose dependent⁶⁹. Isefuku et al. concluded that gentamicin may be detrimental to bone repair in vivo and vitro⁷⁰. Others in vitro work have shown that rifampicin at doses used in clinical practice can inhibit the proliferation of osteoblast-like cells⁷¹. While antibiotics remain an important part of trauma care in preventing infection, the clinician should be aware of these studies which indicate that it is prudent to avoid high doses of ciprofloxacin, rifampicin and topical gentamicin in order to minimise the risk of nonunion. Additional work is required to investigate the whole range of antibiotics used in fracture patients⁷².

Treatment variables

Quality of reduction: Majority of fractures heals satisfactorily without surgical intervention and only requires a cast or simple immobilization. However, certain fractures require reduction and stabilization. Dur-Nyasad (poor reduction) with a gap at the fracture site adversely affects healing. Sushruta has said that fractures which are not properly reduced are difficult to heal and prognosis will be bad⁷³. Animal studies reveal that a gap of more than 2 mm inhibits bony healing.^{74, 75} The size of the gap has been shown to directly affect revascularization and tissue differentiation in callus in the bovine metatarsal⁷⁶.

Quality of stabilization (Bandhana) and early movements (Sankshobha): Fracture requires the immobilization of fragments for healing. This is achieved by application of certain immobilization means for a particular time period. If immobilization is improper (Dur-Nir- Bandhanad)⁷⁷ i.e. too loose (Shithila Bandha) or too tight (ghaada bandha) either will not serve the purpose or will cause complications. A clinician should refrain from such treatment and patient as well. If early undesirable movements (Sankshobhad) are practiced will disturb the healing process⁷⁸. Mechanical environment provided for secondary healing to progress during fracture repair should allow a degree of movements but not an excess or instability, which will inhibit fracture repair. This represents a fine balancing act which trauma surgeons face as part of their daily routine⁷⁹. Stabilization can facilitate fracture healing by preventing repeated disruption of repair tissue. Fracture stabilization appears particularly important when there is extensive soft tissue injury; blood supply to the fracture margins is marginal and intra-articular fractures. Excessive motion secondary to ineffective stabilization, repeated manipulation, or excessive loading and motion retards fracture healing and may cause non-union or delayed union. In these injuries it is probable that the repeated excessive motion disrupts the initial fracture hematoma or granulation tissue, delaying or preventing formation of fracture callus. A hypertrophied callus response

suggests impaired fracture fixation. If excessive motion continues, a cleft forms between the fracture ends, and a pseudo-arthritis develops⁸⁰.

Other variables

Seasonal variation: Sushruta has indicated towards the seasonal effect upon the healing of a fracture. It has been stated that 'Shishir Ritu' (late winter season from mid January to mid March) is the best season for fracture healing⁸¹. During this season the environmental temperature remains low. According to Ayurved Jathragni (digestive power) is high in this season and is helpful for the formation of Dhatus (tissues) and provides the material for healing. In experimental studies also it has been found that intake of the food, its absorption and metabolism improve during the fall in environmental temperature⁸². Cold temperature also enhances the production of BAT (brown adipose tissue) which modulates the insulin activity in humans and beneficial for the glucose metabolism in the body⁸³. Improved insulin activity and good carbohydrate metabolism can cater the increased energy requirements during fracture healing and thus are beneficial for bone healing. Conversely, A.G.S.A. Mostafa et al. in their experimental studies have shown adverse effect of lower environment temperature on the bone healing. However, while concluding they have questioned that is this also possible in humans or not⁸⁴.

CONCLUSION

In Ayurveda a wide spectrum of intrinsic and extrinsic factors influencing the fracture healing has been described. Some of these factors may have an influence throughout the repair process whereas others may only act during certain stages of fracture healing. Most of these factors are same as has been mentioned in modern literature with scientific validation. But still there are certain variables like Prakriti, Seasonal influence, associated diseases viz. Kushtha (Skin diseases) and Shwas Roga (Respiratory diseases) etc, which are not found in modern literature and require the attention of clinicians and scientists for their clinical application, research and scientific validation today. For the successful management of fractures, a thorough knowledge of all these factors is of paramount importance. Some of the factors such as injury variables, climatic conditions are inevitable; but there is a major group of factors that can be modified to promote the healing process effectively viz. diet, physical & mental status, a proper treatment of concomitant diseases. Similarly proper consideration of the treatment variables will help the surgeon to attain his goal of ensuring an easy and un-hindered fracture healing. Hence, by an intelligent modification of these factors, easy & early fracture healing without undue complications can be achieved.

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