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Review article

Fracture healing in the elderly: A review

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ABSTRACT

Older patients are commonly at a higher risk of experiencing a bone fracture. Complications during fracture healing, including delayed union and non-union, can arise as a result of a multitude of patient and treatment factors.

This review describes those factors which contribute to a greater risk of delayed union and non-union with particular reference to the elderly population and discusses therapies that may enhance the fracture healing process in the hope of reducing the incidence of delayed union and non-union.

Increasing age does seem to increase the risk of delayed union or non-union. In addition, smoking and the treatment of post-fracture pain with non-steroidal anti-inflammatory drugs (NSAIDs) put the patient at the greatest risk, while ultrasound therapy appears to be a non-invasive, effective treatment option to reduce the risk of delayed union or non-union. The use of growth factors and of stem cells and the role of surgery are also discussed.

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1. Introduction

Bone fractures are common in the elderly, with residual lifetime fracture risk in a person aged 60 years reported to be 29% in males and 56% in females [1]. During normal fracture healing, an intricate series of physiological events results in the formation of new bone with structural and mechanical properties similar to that of the original, intact bone [2]. This process results from the release of inflammatory cytokines and growth factors and the migration and differentiation of mesenchymal progenitor cells at the site of injury. Bone healing can be simplified into three successive stages: inflammation, repair, and remodelling. The fracture disrupts the continuity of the bone and ruptures blood vessels, leading to the immediate formation of a clot and the release of biochemical messengers at the fracture site. This results in granulation tissue formation with migration of inflammatory and mesenchymal progenitor cells. During the repair stage, callus develops in which progenitor cells differentiate into either chondrocytes or osteoblasts to deposit cartilage or woven bone, respectively, across the fracture site. Finally, remodelling occurs over a period of months to years during which the callus is modified and replaced by lamellar bone [3].

The normal healing time of a fracture varies from 4 weeks to more than 16 weeks depending on the location, the mechanism of injury, and the degree of soft tissue disruption. In addition, there are a number of intrinsic and extrinsic host factors which are associated with delayed union [4]. In these cases, one or more stages of the healing process are impaired compared to healthy patients, requiring pharmacological or surgical intervention to improve healing rates.

The prevalence of delayed healing and non-union varies greatly between studies, with reported incidence as low as 1% and as high as 54% [5]. In a review of tibia fractures, Phieffer et al. combined the results of 22 studies and found that, among 5517 fractures, 2.5% progressed to non-union while 4.4% underwent delayed union [6]. Such healing complications are a burden for both the patient and the healthcare system. Patients suffer due to a lack of functional healing and are often unable to return to work or to perform activities of daily living. Antonova et al. found the median cost of care for patients in the USA with non-union to be US$25,556 compared to $11,686 for patients without non-union [7], while Patil et al. calculated a direct healthcare cost of nearly £30,000 for treatment of each patient with non-union [8]. Patients are also more likely to be prescribed strong pain medications such as opioids and to require opioid therapy for significantly longer than patients without non-union [7]. Although many cases of delayed union and non-union are idiopathic in nature, several reports have suggested that these complications are more common in the elderly [9–11].

The aim of this literature is to investigate the effect of patient characteristics, such as age and comorbidities, on poor fracture healing and to recommend clinical strategies that could lower the incidence of delayed union and non-union.

2. Methods

A literature search was performed using PubMed and Google Scholar with the key search terms “fracture healing”, “delayed union”, “non-union”, “the elderly”, “pharmacological effects”, “smoking”, “diabetes”, and “acceleration”. Selection criteria for inclusion in this review are as follows: (1) delayed union and/or non-union are the primary clinical outcomes being measured; (2) the study states how it defined delayed union or non-union; (3) a minimum study population of 20 subjects (i.e. no case studies were included); (4) in clinical studies, a minimum patient follow-up time of 12 months; (5) the study is written in English.

2.1. Definitions

There are no clear-cut definitions for non-union and delayed union; because of this, diagnosis can be subjective and varies with the fracture pattern. Methods of diagnosis include radiographic examination, functional considerations (e.g. pain free on weight bearing), or comparison to a control group depending on the diagnosing author or physician. Due to this lack of congruity across studies inspecting delayed union and non-union, this review includes the results of each study based on its own definitions of these healing complications. For clinical studies reported in this review, delayed union is defined as a statistically significant difference in fracture healing times between a group of patients sharing a characteristic (e.g. age above 70 years or smokers) and a control group of healthy patients. A diagnosis of non-union was determined by a lack of radiographic improvement.

3. Age, lifestyle, and comorbidities and bone healing

3.1. Age

With increased age, the majority of the population undergoes physiological changes, such as the development of osteoporosis, that leave them more susceptible to fractures and subsequent healing complications [9]. This is particularly true of female patients post menopause. However, few large clinical studies have examined the influence of age alone on the rate of bone healing after a fracture. Nikolaou et al. conducted a study which found that patients aged 65 years and above have significantly longer healing times than patients aged 18–40 (19.38 weeks vs. 16.19 weeks, respectively) [12]. However, all patients in the elderly group showed radiographic signs of osteoporosis compared to none in the younger group and the female to male ratio was significantly higher in the elderly group. Thus, the study was inconclusive as it did not determine whether ageing, osteoporosis, gender, or a combination may contribute to a delay in healing. In other studies, increased age was correlated to healing complications in tibial shaft [13], clavicle [14], and femoral neck [15] fractures and floating knee injuries [16].

Delayed healing in elderly patients has been attributed to a lower capacity for mesenchymal progenitor cell division and differentiation, impaired angiogenesis, and reduced levels of growth factors with increased age [9]. These findings have been shown in various animal models. Several studies examining the biomechanical progression of fractures have shown that elderly rats require more time to regain full mechanical strength compared to young rats [17–19]. Lu et al. observed the molecular, cellular, and histological progression of tibia fractures in juvenile, middle-aged, and elderly mice and found that young mice showed earlier signs of chondrocyte maturation, vascular invasion, and bone formation at the site of the fracture than elderly mice [11]. The results suggest that enhancing cell differentiation and improving osteoblast