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Correlation of nutritional parameters in long bone diaphyseal fracture healing

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Abstract

Purpose: To study whether the nutritional status of the patient has any effect on the outcome of fracture healing. To correlate various clinical and biochemical parameters for assessment of nutritional status with union of fracture.

Material and Methods: One hundred and two patients having diaphyseal fractures of various long bones were followed prospectively for two years. The patients were categorized into 'malnourished/ undernourished' and 'nourished' status according to the anthropometric markers like body mass index, triceps skin fold thickness and mid arm muscle circumference; and biochemical markers like Hemoglobin, serum albumin, serum transferrin, serum ferritin and creatinine-height index. These fracture was evaluated clinically and radiologically for healing.

This union time or quality of union was correlated with the anthropometric and biochemical parameters.

Results: Femoral diaphyseal fractures were the commonest fracture identified (n=35, 34. 31%) followed by radius and ulna (28%), tibia and fibula (25%) and humanus (12%). High velocity road traffic accident was the most common mechanism of injury seen in 49 fractures (48.04%) followed by fall from height (40%) and Domestic trauma (12%). None of the biochemical parameters showed any correlation for fracture healing. Only Serum Albumin, Creatinine-Height index, Serum transferrin could show significant correlation with malnutrition and poor fracture healing.

Conclusion: Thus our study concluded that serum albumin, serum transferrin and creatinine-height index were good biochemical indicators to predict union time. Anthropometric markers, so commonly considered for assessing deficiency in nutrition, do not correlate with fracture healing significantly and are meant for screening only. Altering the nutritional status while fracture treatment can promote healing.

Keywords: Malnutrition, fracture healing, anthropometric measurements, creatinine-height index

Introduction

The effect of nutrition on medical and surgical outcome in clinical situations has been studied since the late 1930s. The incidence of malnutrition in hospitalized patients is often verified as pre-existing or untreated, and gets compounded during hospitalization. Injury and intervention alter nutrient ingestion and absorption or metabolic requirements, or both. *Jensen et al* reported that patients undergoing orthopedic surgical procedures were found to have an average incidence of clinical and subclinical malnutrition of 42.4 % per patient [1]. Trauma and major surgery were shown to induce a state of malnutrition and a loss of immunocompetence. Prevalence of malnutrition, particularly undernutrition, increases with advancing age. In vitro studies conducted in the elderly have shown that administration of calcium and vitamin D can reduce femoral bone loss and, in institutionalized patients, lower the incidence of hip fracture [2]. A hypermetabolic state thus created needs adequate supplementation with exogenous nutrient substrates which are essential to protect the patient from excessive net protein catabolism and to meet this increased energy requirement. Severe trauma is often followed by a period of food deprivation accompanied by an increased demand by the body for metabolic fuels adding to the impaired hormonal and cellular immunity. Under-consumption of minerals like zinc, silicon, calcium and phosphorus and vitamins may affect fracture healing [3-6].

Total protein, hemoglobin, albumin, total lymphocyte counts, transferrin, ferritin levels and Delayed hypersensitivity have been used as nutritional markers [7-8-9].

Weight loss, triceps skin fold, mid arm muscle circumference, creatinine-height index, serum complement level, serum Immuno-electrophoresis, lymphocyte-T rosettes formation, neutrophil migration, and delayed hypersensitivity have been propounded for nutritional assessment [9-16] When there all these markers are important individually or in any co-ordination in fracture healing remains to be studied. There are only limited studies on the role of improved nutrition in the process of healing of fractured human bones. We hypothesized that whether nutritional status of an individual has a bearing on the timing of fracture healing and whether there is any correlation of various anthropometric clinical or biochemical markers of nutrition with union in various diaphyseal fractures.

Material and Methods

A prospective study was carried out in 102 patients of various age groups between September 2007 to December 2009. Most of the patients in the study group were adults between 18-40 years age group (n=50; 49. 02%) and less than 5 years age group were least (n=3; 2.94%). Femoral diaphyseal fractures were the commonest fracture identified (n=35, 34. 31%) followed by radius and ulna (28%), tibia and fibula (25%) and humanus (12%). High velocity road traffic accident was the most common mechanism of injury seen in 49 fractures (48.04%) followed by fall from height (40%) and Domestic trauma (12%).

The patients were categorized into 'malnourished/ undernourished' and 'nourished' status according to the anthropometric (Body mass index, triceps skin fold thickness and mid arm muscle circumference) and biochemical markers (Hemoglobin, serum albumin, serum transferrin, serum ferritin and creatinine-height index) at the time of admission for treatment of their fractures and then the correlated with the time of fracture healing managed either operatively or non-operatively.

Skin fold thickness was measured, as described by *Frisancho* i.e. at the point marked in ink with the help of measuring tape, midway between the angle of the acromion and the upper border of the ulna with an extended elbow [18].

The mid arm muscle circumference was measured each time at the same point with the help of a measuring tape measure just distal to the marked point, and the mid arm muscle area was calculated with following formula:

MAC x (3.14 x TSFT)] / 4 X 3.14!

(MAC= Mid arm circumference; TSFT= Triceps skin fold thicknes)

Patients with values greater than the tenth percentile of the normal values for the same age group and gender were considered as 'nourished'. Creatinine – height index was calculated as the patient's 24-hour excretion of urinary creatinine in relation to the 24-hour urine creatinine excretion of a normal adult of the same height and gender.

Patients with serum albumin > 3.5 gm%, serum transferrin > 199 mg% and total lymphocyte count > 1500 / cumm were categorized into the nourished group. Patients with normal range of serum ferritin (Males 25-380ng/ml and females 15-150ng/ml), were considered to be nourished.

All investigations were sent on the day of admission and at the end of 6th, 10th, 14th week and 6 months. The subject selection in this study was in accordance with the declaration of Helsinki and the methodology approved by Institutional Ethical Committee. Informed consents were taken from the patients in the study group. Fracture healing was assessed clinically be observing tenderness, abnormal mobility, presence or absence of transmitted movements before standard radiographs were taken to confirm union. No supplemented dietary regime was instituted so that the nutritional intake of patients was not changed.

Results

It was observed that the anthropometric markers remained unchanged from the pre- treatment status for all patients in all age groups. Most patients in the study were underweight (80 cases; 78.43%) and the rest were distributed in the starvation, normal and overweight categories.

Table 1: Assessment of fracture healing with anthropometric parameters.

Groups	No. of patients	Normal union (%)	Delayed union (%)	Nonunion (%)
I – Tsft (mm) values (a) males	**(N=72)**			
1) severe < 2.5 mm	0 (0 %)	0 (0 %)	0 (0 %)	0 (0 %)
2) moderate 2.5-6.0 mm	3 (4.17%)	2 (66.67%)	1 (33.33%)	0 (0 %)
3) mild 6.0 – 12.5 mm	3 (4.17%)	2 (66.67%)	1 (33.33%)	0 (0 %)
4) normal >12.5 mm	66 (91.66%)	26 (39.39%)	36 (54.55%)	4 (6.06%)
(B) females (N=30)				
1) severe < 3 mm	0 (0 %)	0 (0 %)	0 (0 %)	0 (0 %)
2) moderate 3 – 6 mm	0 (0 %)	0 (0 %)	0 (0 %)	0 (0 %)
3) mild 6 – 16.5 mm	20 (66.67%)	4 (20%)	15 (75%)	1 (5%)
4) normal > 16.5 mm	10 (33.33%)	1 (10%)	9 (90%)	0 (0 %)
Ii – Mamc (cm) values (a) males	**(N=72)**			
1) severe < 10 cm	3 (4.17 %)	2 (66.67%)	1 (33.33%)	0 (0 %)
2) moderate 10 – 20 cm	5 (6.94 %)	2 (40%)	3 (60%)	0 (0 %)
3) mild 20 – 25 cm	23 (31.94 %)	7 (30.43%)	15 (65.22%)	1 (4.35%)
4) normal > 25 cm	41 (56.94 %)	19 (46.34%)	19 (46.34%)	3 (7.32%)
(B) females	**(N=30)**			
1) severe < 9 cm	0 (0 %)	0 (0 %)	0 (0 %)	0 (0 %)
2) moderate 9 – 18.5 cm	5 (16.67 %)	0 (0 %)	5 (100%)	0 (0 %)
3) mild 18.5 – 23 cm	12 (40 %)	2 (16.67%)	9 (75%)	1 (8.33%)
4) normal > 23 cm	13 (43.33 %)	3 (23.08%)	10 (76.92%)	0 (0 %)
Iii – Bmi values (kg/m^2)	**(N=102)**			
1) starvation (<14.9)	4 (3.92 %)	0 (0 %)	4 (100%)	0 (0 %)
2) underweight (15 -18.4)	80 (78.43 %)	32 (40%)	44 (55%)	4 (5%)
3) normal (18.5 - 22.9)	14 (13.73 %)	3 (21.43%)	10 (71.43%)	1 (7.14%)

4) overweight (23 - 27.5)	4 (3.92 %)	0 (0 %)	4 (100%)	0 (0 %)
5) obese (27.6 – 40)	0 (0 %)	0 (0 %)	0 (0 %)	0 (0 %)
6) morbidly obese (> 40)	0 (0 %)	0 (0 %)	0 (0 %)	0 (0 %)

Table 1

Assessment of fracture healing with anthropometric parameters. We did not find BMI i.e., weight to the ratio of square of the height, to be any important marker for delayed or nonunion in our study as very few patients had a normal union time (n=35; 34.31%). No correlation of fracture healing could be made with this parameter ($p>0.01$).

The hemoglobin levels showed no correlation as the fracture union was comparably distributed among normal union, delayed union and non-union in both nourished and malnourished categories. It was ethically, although, to make therapeutic efforts to improve the hemoglobin in significantly anemic patients having diaphyseal fractures.

On evaluating the levels of creatinine height index as a biochemical marker, it was observed, nearly half (n=20; 44.44%) of the patients with creatinine height index > 0.9 mg% united in time, and 51.11% (n=23) had delayed union in comparison to a higher percentage of delayed union among the malnourished group (n=39; 68.42%). Creatinine height index was correlated as a significant marker affecting union time ($p<0.01$) as do serum albumin levels.

Serum transferrin level as a marker for nutritional status, majority of the patients were labeled malnourished (n=57; 55.88%). When this parameter was assessed for its correlation with fracture healing it was observed that majority of the patients in the nourished category had a normal union (n=23; 51.11%) and however in the malnourished category maximum number of the patients had delayed union and few also proceeded to non-union (n=4; 7.02%). This observation was found significant ($p<0.01$).

The values of serum ferritin for assessing the nutritional status for males and females are different and no significant co-relation of serum ferritin with union time of fracture in both genders.

Table 2: Correlation of biochemical parameters with fracture healing.

Group		No. of Patients (N=102)	Normal Union (%)	Delayed Union (%)	Non- Union (%)
I – Hemoglobin (gm %)					
a)	Normal (12.5–14.5 gm %)	16 (15.69%)	8 (50%)	7(43.75%)	1 (6.25%)
b)	Mild (9.5 – 12.4 gm %)	85 (83.33%)	27 (31.76%)	54 (63.53%)	4 (4.71%)
c)	Severe (8–9.4 gm %)	1 (0.9%)	0 (0%)	1(100%)	0 (0%)
d)	Very severe (< 8 gm %)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
II - Creatinine-height index (mg %)					
a)	< 0.9 mg % (malnourished)	57 (55.88%)	15 (26.32%)	39 (68.42%)	3 (5.26%)
b)	> 0.9 mg % (nourished)	45 (44.12%)	20 (44.44%)	23 (51.11%)	2 (4.44%)
χ^2 =14.246, χ^2 (2,0.01) = 9.210, $p<0.01$*					
III - Serum albumin (gm %)					
a)	< 3.5 gm % (malnourished)	44 (43.14%)	6 (13.64%)	36 (81.82%)	2 (4.5%)
b)	> 3.5 gm % (nourished)	58 (56.86%)	29 (50%)	26 (44.83%)	3 (5.17%)
χ^2 =10.99, χ^2 (2,0.01) = 9.210, $p<0.01$*					
IV-Serum transferrin (mg %)					
a)	<199mg % (malnourished)	57 (55.88%)	12 (21.1%)	41 (71.93%)	4 (7.02%)
b)	>199 mg % (nourished)	45 (44.12%)	23 (51.11%)	21 (46.67%)	1 (2.2%)
χ^2 =11.24, χ^2 (2,0.01) = 9.210, $p<0.01$*					
V - Serum ferritin (ng /ml)					
(A)	**Males**	**(N=72)**			
a)	<20 ng/ml (malnourished)	32 (44.44 %)	14 (43.8%)	18 (56.2%)	0 (0%)
b)	20-300 ng/ml (nourished)	40 (55.56 %)	16 (40%)	20 (50%)	4 (10%)
χ^2 =7.99, χ^2 (2,0.01) = 9.210, p>0.01					
(B) Females		**(N=30)**			
a)	<18 ng/ml (malnourished)	21 (70 %)	3 (14.29%)	18 (85.71%)	0 (0%)
b)	18-200 ng/ml (nourished)	9 (30 %)	2 (22.22%)	6 (66.66%)	1 (11.11%)
χ^2 =5.25, χ^2 (2,0.01) = 9.210, p>0.010					

Discussion

Malnutrition is common in hospitalized injured patients and is known to delay fracture healing and increase morbidity [19-20]. A good nutrition and nutritional supplements are required for augmenting musculoskeletal recovery after a fracture.

Studies in rat models have shown that mechanical properties of fracture callus is proportionately dependent on protein and mineral consumption in later course of normal fracture healing. Dietary intervention in the immediate post fracture period reverses the detrimental influence of protein deprivation on fracture healing [21-23]. Other in vitro reported that the healing process for bone fractures is sensitive to mechanical stability and blood supply at the fracture site[24]. Sinha *et al* (2009) [25] assessed the effects of amino acids; lysine and arginine on fracture healing in rabbit model and demonstrated their beneficial effects by improved angiogenesis and collagen synthesis at fracture site in early stages of fracture healing [25]

Low protein intake appears to play a distinct detrimental role in the management of hip fractures and their complications. Patterson and Magnus *et al* in separate studies showed that comprehensive balanced nutrition supplement (1000 kcal daily intravenous supplement for 3 days, followed by a 400 kcal oral nutritional supplement for 7 days) resulted in lower complication rates and mortality at 120 days postoperatively in healthy patients with hip fracture [13-26]. In contrast, Olofsson *et al* conducted a randomized controlled trial in 157 older patients with femoral neck fracture and found no detectable significant improvements regarding nutritional parameters between the dietary intervention and the control group at the four-month follow-up but men improved their mean BMI, body weight and MNA scores in both the groups while women deteriorated in both groups [27].

Substantial unrecognized malnutrition exists in the surgical patient population. Evaluation of various nutritional parameters may help assessment of operative morbidity and mortality in the malnourished operative candidate. Our data showed a correlation of poor fracture healing in hypoalbuminemia patients. Mullen *et al* also found serum albumin level along with serum transferrin level, and delayed hypersensitivity reactions as the only accurate prognostic indicators of postoperative morbidity and mortality. However, we randomized our patients for operative and non-operative management [10].

Cut-off level of optimum concentration serum albumin has been shown by Dreblow *et al.* of less than 3.5 g/dl had a longer-than-average hospital stay [11]. *Mark et al*. Also concluded that a more aggressive approach to nutritional support is needed for the hypoalbuminemia patient with a hip fracture, particularly for those with a serum albumin below 3.0 [12]. Recent trials used serum albumin and total leukocyte count as a predictor for poor outcome in hip fracture in elderly or joint replacement surgery. An albumin level of <3.5 grams/deciliter was predictive for increased length of stay (p=0.03) and for in-hospital mortality (p=0.03) [14-15]. A total lymphocyte count < 1,500 cells/milliliter was predictive for one-year mortality ($p < 0.01$). Total leucocyte count was not taken in our population for assessment of nutritional status because of many reasons, firstly, due to temperate climatic conditions, our patients tend to suffer from subclinical infections like Malaria, GI infections, UTI or ENT infections which can alter the TLC at a given time. For the same reason Delayed type of hypersensitivity reactions like the tuberculin /Montoux test was not applicable in the study as prevalance of infection of tuberculosis is high in our patients however, incidence is reducing because of NTCP and DOTS regime.

Application of Hemoglobin as a marker of nutrition, Gruson *et al*. found anemic population (Hb≤ 12%) are at risk for poor outcomes, in form of longer in hospital stay and mortality rate at six and twelve months after hip fracture. With this criteria majority of our patients were mildly anemic (Hb 9-12.5 gm %) but it failed to show any statistical significance with fracture healing [28].

Dwyer *et al.* in two separate studies on young patients with lower limb trauma propounded that wound healing was earlier when creatinine-height index was normal throughout the course of treatment and was delayed when serum albumin level was low. Our results are also supportive to this observation that patients with creatinine-height index >0.9 mg% had uneventful fracture healing [16].

Fracture healing requires more energy than one might expect. Thus, it is also appropriate to increase the caloric intake to promote healing. In traumatic fractures of the long bones, for example, there is an immediate increase in metabolic demands that can translate into a caloric demand three times that of normal. While a normally active adult may require 2,500 calories a day, a bedridden, injured patient with multiple fractures may need 6,000 calories per day, if this demand is not met, the healing process is compromised [29-30].

Although it is empirical to maintain good nutrition in fracture patients in an orthopedic ward, many patients fall short of normal parameters by anthropometric or biochemical markers. With limited resources available for hospital diet in a tertiary hospital, the provision of good nourishing diet becomes a major issue financially for a family during the treatment of fracture of a family member. Justification of a financial expenditure on nutritious diet over and above the cost of quality medicine and implants is a major concern for poor socio-economic strata of our population with limited resources. Prolonged stay in the hospital for recovery, as is characteristic fracture patients, puts an objective perspective towards the role of nutritional status in fracture healing.

The study has shown a significant observation that anthropometric markers, so commonly considered for assessing deficiency in nutrition does not correlate with fracture healing. However, it cannot be concluded that anthropometric markers, so commonly taken as criteria for undernourishment and malnourishment are objectively not reliable criteria for wound and fracture healing. These are screening criteria which will manifest clinically in later stages of malnutrition, however, not in those with undernutrition, when internal metabolism has compensated. There are limitations to our study, our groups were not normally distributed, and however, we attempted to include patients of all age groups in the study cohort. Fracture healing patterns are different in adults and children, severity of malnutrition seems to affect fracture healing in children more than adults, but data deciphered in our study is insufficient to prove this. Secondly, we haven’t categorized malnutrition by some kind of scoring system/grading system to get a proper control group. Most of our patients were undernourished or normally nourished but post-traumatic catabolism has led them to a state of undernourishment. This is a grey zone population which can confound our results.

Our study concludes that serum albumin, serum transferrin and creatinine-height index were good biochemical indicators to predict union time and had a significant correlation with fracture healing (p<0.01) and whereas no other biochemical marker studied were found to bear any significant correlation with fracture healing. The study has shown a significant observation that anthropometric markers, so commonly considered for assessing deficiency in nutrition does not correlate with fracture healing.

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