RADIOGRAPHIC EVALUATION OF NECK SHAFT ANGLE (NSA) REMODELLING FOLLOWING VARUS OSTEOTOMY OF PROXIMAL FEMUR IN CHILDREN

by

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ABSTRAK

<u>BahasaMelayu</u>

Pendahuluan :

Sudut leher tulang femur (NSA) berkurang mengikut umur denganpurata 145˚ pada 1-2 tahun, 134˚ pada 6-8 tahun dan 120-125˚ semasa dewasa. Apabila sudut leher tulang femur(NSA) diturunkan secara pembedahan sebagai rawatan untuk masalah tulang pinggul, proses pembentukan semula akan membetulkan perubahan ke arah sudut leher tulang femur (NSA) normal untuk umurnya.

Kaedah :

Ini adalah satu ‘cross-sectional study’, dilakukan ke atas pesakit yang telah menjalani pembedahan ‘varus osteotomy’, sejak 2003 sehingga 2010 di hospital kami. Di dalam tempoh kajian, 22 pinggul yang telah menjalani pembedahan proksimal‘ varus osteotomy ’telah diukur sudut leher tulang femur (NSA) oleh penyelidik berdasarkan radiograf pelvik di sistem PAC.

Titik penilaian berada pada sebelum pembedahan, sejurus selepas pembedahan, akhir tahun pertama, akhir tahun kedua dan akhir tahun ketiga selepas pembedahan.Purata 3 bacaan pada selang seminggu diambil sebagai sudut leher tulang femur (NSA) pada setiap titik bacaan.

Keputusan :

Terdapat 22 pinggul terlibat di dalam kajian ini.Pesakit adalah di antara umur 1 tahun 10 bulan sehingga 10 tahun 10 bulan(purata umur : 5 tahun 6 bulan). Sudut leher tulang femur telah diukur pada tahun pertama dalam kalangan 22 pesakit, pada tahun kedua dalam kalangan 16 pesakit dan tahun ketiga dalam kalangan 11 pesakit. Jumlah tambahan 'varus' dibuat adalah di antara 11˚ hingga 66˚ dengan purata sebanyak 115.68˚.

Kebolehpercayaan ukuran NSA yang dibuat oleh penyelidik adalah bagus dengan nilai ICC ('intra-observer') sebanyak 0.932 .

Pada tahun pertama selepas 'osteotomy', daripada 22 pinggul, sudut leher tulang femur(NSA) menurun dalam kalangan 9 pinggul dan meningkat dalam kalangan 13 pinggul yang lain(59.1%). Pada tahun kedua selepas'osteotomy', sudut leher tulang femur meningkat (diantara 2˚ hingga 17˚) pada 14 daripada 16 pinggul. Pada tahun ketiga selepas pembedahan, sudut leher tulang femur meningkat(diantara 2˚ hingga 16˚) pada 9 daripada 11 pinggul. Hanya terdapat satu pesakit yang Berjaya mencapai sudut leher tulang femur asal dalam tempoh 3 tahun.

Tidak ada korelasi sudut leher tulang femur pembentukan semula dan umur pada 'osteotomy'.

Analisis korelasi Pearson untuk 13 pinggul dengan peningkatan sudut leher tulang femur pada tahun pertama selepas 'osteotomy' menunjukkan korelasi positif yang kuat(r = 0.455) di antara jumlah tambahan varus dan pembentukan semula.

Analisis korelasi ‘Pearson’ untuk 13 pinggul dengan peningkatan sudut leher tulang femur pada tahun pertama menunjukkan korelasi negative sederhana(r=-0.360) di antara sudut pada pembetulan dan pembentukan semula.

Kesimpulan :

Sudut leher tulang femur di kebanyakan pinggul meningkat selepas ‘varus osteotomy’ tetapi tidak berjaya mencapai sudut asal di dalam tempoh 3 tahun. Pinggul yang mengalami penurunan sudut leher tulang femur di akhir tahun pertama, didapati mengalami peningkatan sudut leher tulang femur di dalam tahun-tahun yang berikutnya. Umur pada masa ‘osteotomy’ tidak mempengaruhi jumlah pembentukan semula.Terdapat hubungan positif di antara jumlah‘varus’ di buat dengan jumlah pembentukan semula sudut leher tulang femur.

ABSTRACT

Bahasa English

Introduction :

The neck shaft angle (NSA) of the proximal femur decreases from average as 145˚ at 1-2 years, 134˚ at 6-8 years, and 120-125˚ in adulthood. When the NSA is surgically reduced for treatment of hip problems, the remodelling process will correct the changes towards its normal NSA angle for the age.

Methodology :

This was a cross-sectional studyconducted on patients who had undergone varus osteotomy between 2003 and 2010 in our hospital. In the period of this study, 22 hips who had undergone proximal varus osteotomy was measured for the neck shaft angle (NSA) by the researcher based on pelvic radiograph on PAC system. The point of assessments were at pre-operative, immediate post operative, end of one year, end of second year and end of third year post operative. Mean of three measurement at one week interval was taken as NSA at each measurement point.

Results:

There were 22 hips included in this study. The patients were between age of 1 year 10 months till 10 year 10 months (mean age : 5 year 6 months). The neck shaft angle was measured at one year in 22 patients, at two years in 16 patients and at three years in 11patients. . Amount of additional varus created between 11^0 to 66^0

with mean of 31.2^0 . The range of NSA created by the surgerywas between 93^{0}and 136^0 with mean of 115.68$^{0.}$

There was a good realibility for measurement of NSA done by the researcher with intra-observer ICC of more than 0.932 .

In the first year after osteotomy, out of 22 hips , NSA decreased in 9 hips and increased in other 13 hips (59.1 %) . In the second year after osteotomy NSA increased (between 2^0 and 17˚) in 14 out of 16 hips . At year three after surgery NSA increased (between 2^0 to 16) in 9 of 11 hips . There was only one patients able to achieve original NSA within 3 years.

Pearson correlation analysis of 13 hips with increase of NSA at one year after osteotomy showed a strong positive correlation (r=0.455) between amount of additional varus and remodelling.

Pearson correlation analysis on 13 hips with increased NSA at the end of year one, showed a moderate negative correlation (r=-0.360) between angle at correction and remodelling.

Conclusion :

NSA in most of the hips increased after varus osteotomy but was not able to reach original angle within 3 years. The hips with decrease NSA at the end of year one, had increased NSA in the following years. The age at time of osteotomy did not influent the amount of remodelling. There was a positive correlation between amount ofvarus created with the amount NSA remodelling.

RADIOGRAPHIC EVALUATION OF NECK SHAFT ANGLE (NSA) REMODELLING FOLLOWING VARUS OSTEOTOMY OF PROXIMAL FEMUR IN CHILDREN

Abstract

Introduction : The neck shaft angle of the proximal femur following varus osteotomy will change towards its normal NSA angle for the age. This study was conducted to find the changes of proximal femur following varus osteotomy in children within first three years.

Patients and Methods: This was a retrospective study conducted on 22 femurs following varus osteotomy. The neck shaft angle measurement was done on pelvic radiograph on PAC system. The point of assessments were at pre-operative, immediate post operative, end of one year, end of second year and end of third year post operative.

Results:. The patients were between age of 1 year 10 months till 10 year 10 months (mean age : 5 year 6 months). Amount of additional varus created between 11^0 to 66^0 with mean of 31.2^0 . The range of NSA created by the surgery was between 93^0 and 136^0 with mean of $115.68^{0.}$

In the first year after osteotomy, out of 22 hips , NSA decreased in 9 hips and increased in other 13 hips (59.1 %) . In the second year after osteotomy NSA increased (between 2^0 and 17˚) in 14 out of 16 hips . At year three after surgery NSA increased (between 2^0 to 16) in 9 of 11 hips . There was only one patients able to achieve original NSA within 3 years.

Pearson correlation analysis of 13 hips with increase of NSA at one year after osteotomy showed a strong positive correlation (r=0.455) between amount of additional varus and remodelling.

Conclusion : The age at time of osteotomy did not influent the amount of remodelling. There was a positive correlation between amount of varus created with the amount NSA remodelling. The remodelling did not complete within 3 years.

INTRODUCTION

The neck shaft angle (NSA) of the proximal femur changes with age. It is widest between age of 1 to 3 years (145˚) , get narrower with growth (133˚ at 8-12 years) and achieved 120-125˚ in adulthood. (Kay R.M et al (1), Von Lanz (2). As remodelling occur, narrowed NSA angle following varus osteotomy of proximal femur for treatment of hip problems may gradually get wider to meet normal NSA for the age.

There have been few studies on radiographic evaluation of NSA remodelling following varus osteotomy of proximal femur in children. Thalkani et al (3) and Herceg et al (4) proved that age does not influence remodelling potential post osteotomy. Sangavi et al (5) and Thalkani et al (3) showed the lower post- operative NSA, the greater the remodelling post osteotomy. Karadimas et al (6)studied growth of the proximal femur after varus-derotation osteotomy in the treatment of CDH (Congenital Dislocation of Hip) and found that the NSA improved from varus to the normal range with time. They also found that different NSA remodelled with different amount.

Suda et al (7) reported the NSA of that hips with varus derotation osteotomy of upper femur at age of 1.3 to 5.2 years and age of 8 to 10 years had returned to about 135˚ and was similar to that of unaffected side during follow up period of 10 to 26.2 year.

However these studies looked at final NSA remodelling at many years after the surgery. We conducted this study to find out the changes in first three yearsas it may influence the outcome of surgery in developmental dislocation of hips and Perthes disease.

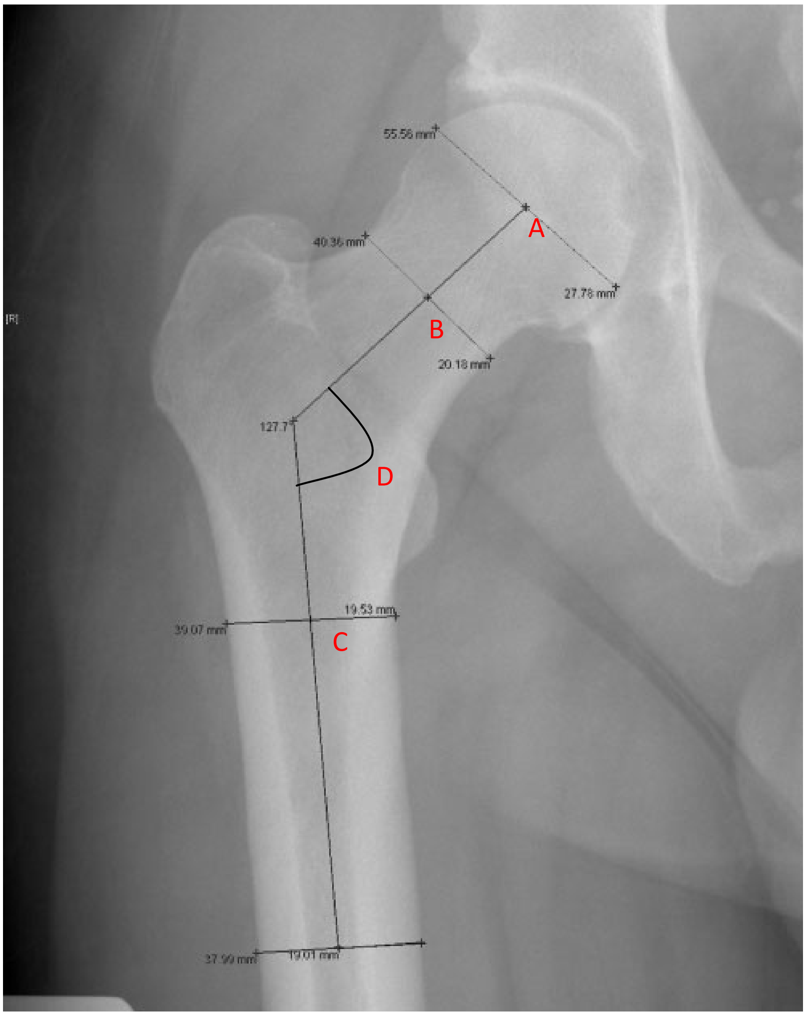
METHODOLOGY

This study was a retrospective studyon patients that had undergone varus osteotomy of proximal femur between 2003 and 2010 in in Hospital University Sains Malaysia (HUSM). They were between age of 2 years – 12 years at the time of surgery
Measurement of NSA on the radiograph using PAC system were done on radiograph taken within one week before operation and within one week post operation as the base line (figure 1). While NSA measurement at one year, 2 years and 3 years after the surgery were taken for comparison with that within one week after surgery to get the NSA changes. To minimise the error, measurements were repeated THREE times at one week interval by one researcher and the average was taken as final reading.

Measurement of NSA on the radiograph was done on PAC system by following steps:

1. The midpoint of the femoral neck at its narrowest point and the centre of the femoral head (A) were identified. Centre of the femoral head was found by halving its maximum diameter using the linear measuring feature.
2. The neck axis was then generated by extending a line through these points. (A, B)

3. The femoral shaft axis was generated by identifying the mid-point of the diaphysis at two different points distal to the flare of the lesser and greater trochanters (C, D), again using the linear measuring feature.
4. The intersection of these two axis was then determined using the angle-measuring feature.(α, representing NSA).



(Figure :Radiograph of proximal femur of right hip joint)

(A : Centre of the femoral head, B : Centre of the femoral neck C : Mid diaphysis, D : Intersection of A, B and C; NSA measured by angle of AD and DC)

(Adapted from Wilson JD(8))

RESULT

This study was done on 20 patients (22 hips) The sample consist of 15 (68.18%) developmental dislocation of the hip (DDH) and 7 (31.82%) Perthes patient. Thirteen of them (59.09 %) were female. The age of patient during osteotomy was in between 1 year 10 months till 10 year 10 months (mean age : 5 year 6 months). The fixations used were dynamic compression plate (DCP) 19 hips and CAPOS (Cannulated Pediatric Osteotomy System) plate in 3 hips.

The ICC (shows intraclass correlation coefficient) of 3 readings, showed value of 0.932 till 0.970. This indicates a strong realibility.

The neck shaft angle was measured at one year in 22 patients . In 9 patients (40.9 %) the NSA decreased between -27˚ to -2˚, while in the other 13 patients (59.1 %), the NSA get wider between 1˚ to 27˚ with mean of 9.69˚. The neck shaft angle was measured at two years in 16 patients . In 9 patients (no 1-no 9), NSA increased further while in 7 patients (no.16 – no. 22) that had decrease NSA at year one showed increment of NSA in second year . The neck shaft angle was measured at three years in 11 patients post operation.Nine of them get the NSA wider between 2^0 to 16^0 with mean of 7˚.The findings showed that at two and three years after surgery NSA became wider in most of the patients but did not reach original NSA. Meanwhile, patient no 21 (one patient)(age of 8.85) did not remodel until end of year two.Mean final correction at three years base on 11 patients was 5.1˚. Mean NSA at 3 years in those 11 patients was 128.5˚. Only 1 out of 11 patient had full correction.

Pearson correlation analysis showed that there was no correlation (r= -0.167) between age of osteotomy and NSA remodelling at 1 year (Figure 5.5.2). Pearson correlation analysis showed that there was moderate correlation(r = -0.330) between age of osteotomy and NSA remodelling at 2 year(Figure 5.6.2) . The changes occur more in patient's age 3 years old and less and the remodelling reduce as the child gets older. Pearson correlation analysis showed that there is weak correlation (R =- 0.235) between age of osteotomy and NSA remodelling at three year .

Regarding correlation between amount of correction with rate of changes of NSA, in this study, amount of additional varus created were between 11^0 to 66^0 with mean of $31.2^{0.}$ However ,we excluded 9 hips with decreased NSA for the purpose of analysis between amount of additional varus and amount of remodelling at end of year one.Pearson correlation analysis of 13 hips with increase of NSA at one year after osteotomy showed a strong positive correlation (r=0.455) between amount of additional varus and changes of NSA.

DISCUSSION

The neck shaft angle (NSA) of the proximal femur decreases with age. Harris et al (9) measured the average as 137˚ at birth, 145˚ at 1-2 years, 143˚ at 2-4 years, 135˚ at 4-6 years, 134˚ at 6-8 years, 133˚ at 8-12 years, and 120-125˚ in adulthood. Other studies showed that the highest mean NSA of 145˚ occurs between 1 to 3 years of age. (Kay R.M et al (1), Von Lanz (2)

When the NSA is surgically decreased for treatment of hip problems like developmental dislocation of the hip (DDH) and Perthes, the healing process will correct the changes towards its normal angle for the age.

This study measure NSA using pelvic x ray which is digitalized into the Centricity EnterpriseTM (GE Healthcare Pty Ltd) picture archiving and communication system (PACS). Even though rotation of hips could not be exactly standardised, this method is still reliable based on study by Marmoor M at el (10) who found that in saw-bone model, femoral neck rotation of less than 35^0 make the measurement NSA measurements varied less than 5^0. In addition to that , Robert M. Kay et al (1) measured NSA on plain radiograph of adult dried femoral specimen between 20° of external rotation and 50° of internal rotation and found that the NSA was within 5° of the true NSA.

Computed tomography (CT) techniques allow accurate 3D bone reconstruction (Subburaj et al , (11)). However, it is very expensive and involve significant radiation, it is not possible for multiple measurement on same subject.(Weiner et al , (12) and Lee et al, (13). In this study, we decided to use x ray since we need to compare angle of the current NSA with post operative NSA angle. Sabharwal et al (14) showed that conventional radiography still mainstay of primary evaluation for misalignment and NSA measurement (Marmor M (10)

Intraobserver reliability of NSA measurement

One observer was used in this study as to improve reliability of measurement. The inter-observer bias was minimised by measuring at three different intervals. In this study, the reliability was very high with an ICC > 0.932. Throughout the study, the final NSA was taken as mean of three separate measurement to improve on the accuracy. There is also another study done by Wilson et al (8), where the author obtained an intra-observer agreement that lie within +/- 2.5˚ (95% CI = +/- 1.7˚ till 3.3˚) by using Bland-Altman plot method.

NSA remodelling with time

In this study, we found that in the first year after osteotomy only 13 patients (59.1%) the NSA get increased. This group of patient underwent remodelling in the first year after surgery.

We think decrease of NSA in the other 9 patients (40.9%) could be due to further changes that occurred during fracture healing in unstable fixation dynamic compression plate (DCP) and screws fixation method. Number of screws proximal and distal to the osteotomy site need to be studied. Furthermore, the narrowing did not occur in three patients with CAPOS (

Cannulated Pediatric Osteotomy System) plate fixation . Unfortunately statistical analysis could not be done due to small sample size.

Other possibilities that beyond control of this study are weight of the patient and level of activity after the surgery. Unfortunately, we are unaware of any studies discussing this co-founding factors.

Avascular necrosis is unlikely to be the cause of this phenomena as it occurs only in the first year after surgery.

In the second and third year after the surgery most of the patients including those with negative changes of NSA in the first year get widening of NSA. At this time the healing has become solid and the remodelling takes place without disturbances. Therefore the factors that influence the changes were analysed based on data collected at year two and year three after osteotomy. We only had 11 out of 22 patients completed the assessment at three years with only one patient remodelled completely.

We are aware that Herceg et al (4) reported that most of the remodelling (40%) occurred within the first years after surgery. Sangavi et al (5) concluded that remodelling was essentially completed at 3 years. Suda et al (7) reported that varus osteotomy done to patient corrects with time but it took more than 5 years to return to normal and was slightly quicker if varus osteotomy were combined with innominate osteotomy. We did not study the association with pelvic osteotomy.

Age at osteotomy and amount of Remodelling

In this study on patients with age at osteotomy between age of 1 year 10 months till 10 year 10 months (mean age : 5 year 6 months), we found that there was no correlation of NSA remodelling and age at osteotomy. This finding is constant with study by Suda et al (7), that in patients age between 1.3 to 5.2 years (mean of 3.1 years), there are no correlation between age of osteotomy and NSA measurement at final examination.

Study by Talkhani et al (3) in patients age between 5 to 8.7 years (mean of 7 years) also conclude that NSA remodelling after varus osteotomy does not dependent on age at operation. Herceg et al (4) who studied Perthes patient, found that there was no statistical difference between patient younger and older than 8 years old .This is in contrast to study done by Sangavi et al (5) that showed in patients between 5 months to 5 years 2 months (mean of 1 year 10 months), NSA remodelling occurred less in older patient .

Age at time of osteotomy between age of 1 year 10 months till 10 year 10 months (mean age : 5 year 6 months) did not influence the amount of remodelling.

In this study, relationship of amount of varus created by the surgery and NSA after osteotomy with amount of remodelling were only analysed on 13 patients with increased NSA because we think the decreased of NSA in the other 9 patients were due to reasons mentioned in section 6.4.

We had a similar findings with other study that the lower the post-operative femoral NSA, the greater the femoral NSA remodelling that occur (Suda et al (7), Sangavi et al (5). Karadimas et al (6) found that the highest percentage of NSA remodelling occur when the NSA were left the angle between 100˚ and 110˚ after the procedure. However we did not see an obvious pattern in our study.

A positive correlation between amount of varus created with the amount NSA increment found in this study proves that remodelling will try to correct abnormality created by the surgery of fracture. A negative correlation of the NSA after osteotomy with the amount of

NSA increment found in this study support the above statement. This evidence also proved that within NSA created by the surgery between 93^0 and 136^0 would increase towards normal angle for the age.

CONCLUSION

NSA of most of the hips increased after varus osteotomy did not reach original angle within 3 years. The age at time of osteotomy did not influence the amount of remodelling.There was apositive correlation between amount of varus created with the amount NSA increment within the limit of NSA the created from 93^0 to 136^0 (mean of 115.68^0.) and mean of additional varus of 31.2˚.Therefore we concluded that the recommended mean additional varus for patient between 1.8 years to 10.8 years is 31.2˚ with the awareness of various remodelling might occur.

CONTENTS

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1.0 INTRODUCTION

Bone remodeling is an adaptive process of the bone undergoing substantial changes in structure, shape and composition. This will occur as part of normal physiological process or part of fracture repair. In children, the remodelling potential is greater due to development of fracture callus is faster (Mosely, 1992) and the periosteum is much thicker compared to adult (Stilli, 2007).

Varus osteotomy of proximal femuris one of the common surgical procedures for hips problem in children. As remodelling occur, narrowed NSA angle created by the surgery will get wider to meet normal NSA for the age. The neck shaft angle (NSA) of the proximal femur changes with age. It is widest between age of 1 to 3 years (145˚) , get narrower with growth (133˚ at 8-12 years) and achieved 120-125˚ in adulthood. (Kay R.M et al in 2000, Von Lanz(1951).

There have been few studies on radiographic evaluation of NSA remodelling following varus osteotomy of proximal femur in children. Thalkani et al (2001) and Herceg et al (2004) proved that age does not influence remodelling potential post osteotomy. Sangavi et al (1996) and Thalkani et al (2001) showed the lower post-operative NSA, the greater the remodelling post osteotomy. Karadimaset al (1982)studied growth of the proximal femur after varus-derotation osteotomy in the treatment of CDH (Congenital Dislocation of Hip) and found that the NSA improved from varus to the normal range with time. They also found that different NSA remodelled with different amount.

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However these studies looked at final NSA remodelling at many years after the surgery. We are interested to find out the changes in first three years as it is associated with early subluxation following surgery of DDH. Furthermore, remodelling process of Perthes disease occurs within one to 3 years of fragmentation phase that require containment.

We conducted this study to find the amount and rate of remodelling of proximal femur in correcting the surgically created additional varus within the first 3 years. The influences from age of patients and amount of varus created on NSA remodelling were also studied. The intra-observer measurement reliability of NSA was also analysed.

2.0 LITERATURE REVIEW

2.1 Neck Shaft angle (NSA)

The neck-shaft angle is the deviation of the femoral neck from the femoral diaphysis, where axes of both structures are co-planar. This is usually measured in a two-dimensional radiograph taken in the antero-posterior (AP) view, which is assumed to be perpendicular to the plane containing the femoral diaphysis and neck.The neck-shaft angle is calculated as the angle between the femoral neck vector and the diaphyseal vector in the plane that contains the diaphyseal vector and the centre of the femoral head.(Doube et al, 2010)

2.2 Normal development of proximal femur (NSA changes)

2.2.1 Intra-uterine

Watanabe et al (1974)outlined a study of hip development in 288 hips from144 embryos and fetuses from 14 to 300 mm C-R (crown - rump) length ending at 24 weeks gestation.The author findings include measurement of neck shaft angle of 130˚ during fetal development.

2.2.2 Neck shaft angle changes from birth till adult

The neck shaft angle of the proximal femur as measured in the anteroposterior plane has also been studied extensively by Watanabe and the author found that the normal neck shaft angle decreases with age.

Harris et al (1976) measured the average as 137˚ at birth, 145˚ at 1-2 years, 143˚ at 2-4 years, 135˚ at 4-6 years, 134˚ at 6-8 years, 133˚ at 8-12 years, and 120-125˚ in adulthood. Von Lanz (1951) showed a similar pattern of change, with the highest mean angle of inclination of 145˚ at 1-3 years of age followed by diminution to a mean of 126˚ at skeletal maturity.

Normal adult values documented are similar to studies from the late 1800s to the mid-twentieth century, indicating values of 124˚, 126˚, 129.6˚, and 126.4˚. Humphrey et al published one of the earliest detailed studies in 1888. The average angle in 30 adult femurs was 124˚ (range = 113˚ - 135˚), in 15 additional femurs from individuals greater than70 years of age it was 123.7˚, and in 30 adult bones from Germany it was 128˚. Hoaglund and Low (1980)noted adult angles NSA of 135˚ in Caucasian and Chinese femurs with no sex variance.

2.2.3 Neck shaft angle study in normal population

Study done by Anderson et al (1998), whereby the author collected data of 30 modern (cadaveric) skeletal remains, historic (medieval) and prehistoric human population samples of neck shaft angle from skeletal remains done by personal measurement and the one that is published by other authors.The data was analysed with respect to sexual dimorphism, bilateral asymmetry, geographical patterning and general economic level. For east Asians (example : Hong Kong, China), the mean neck shaft angle was 136.2˚ with an S.D of 3.6˚.

2.3 Fracture healing and remodelling

2.3.1 Bone as a structure

Bone tissue composed of hydroxyapatite, collagen, small amounts of proteoglycans, non-collagenous protein and water(by Weiner,1998 and Lucchinetti,2001).Inorganic components are mainly responsible for the compression strength and stiffness, while organic components provide tension properties. This composition varies with species, age, sex, the specific bone and whether or not the bone is affected by a disease (Ginebra,2000)

Macroscopically, bone tissue is non-homogeneous, porous and anisotropic. Even though porosity can vary from 5 to 95%, most bone tissues have either very low or very high porosity. There are two types of bone tissue (see Fig. 2.1). The first type is trabecular or cancellous bone with 50–95% porosity, usually found in cuboidal bones, flat bones and at the ends of long bones. The pores are interconnected and filled with marrow (a tissue composed of blood vessels, nerves and various types of cells, whereby their main function is to produce the basic blood cells), while the bone matrix has the form of plates and struts called trabeculae, with a thickness of about 200 μm and a variable arrangement (Martin et al, 1998).

The second type is cortical or compact bone with 5–10% porosity and different types of pores (Cowin, 1999).Vascular porosity is the largest (50 μm diameter), formed by the Haversian canals (aligned with the long axis of the bone) and Volkmann's canals (transverse canals connecting Haversian canals) with capillaries and nerves. Other porosities are associated with lacunae (cavities connected through small canals known as canaliculi) and with the space between collagen and hydroxyapatite (very small, around 10 nm). Cortical bone consists of cylindrical structures known as osteons or Haversian systems (see Fig. 2.2), with a diameter of about 200 µm formed by cylindrical lamellae surrounding the Haversian canal. The cement line formed the boundary between the osteon and the surrounding bone.

Cortical bone is usually found in the shafts of long bones and surrounding the trabecular bone forming the external shell of flat bones. Combination of trabecular and cortical bone forms a ‘‘sandwich-type’’ structure, well known for its optimal structural properties (Currey, 2002).

Bones can grow, modify their shape (external remodelling or modelling), self-repair when fractured (fracture healing) and continuously renew themselves by internal remodelling. All these processes are influenced by mechanical, hormonal and physiological patterns.

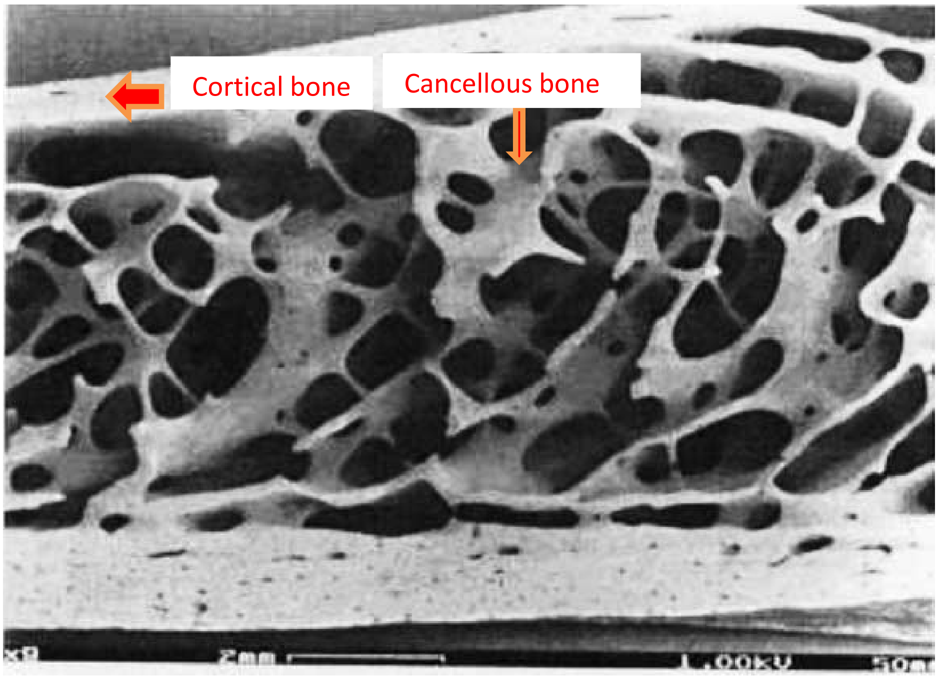

Figure 2.1 shows bone section (macroscopic) that shows two types of bone tissue: cortical and trabecular bone (Adapted from Williams PL. Gray's anatomy. 38th ed. Churchill Livingstone; 1995).

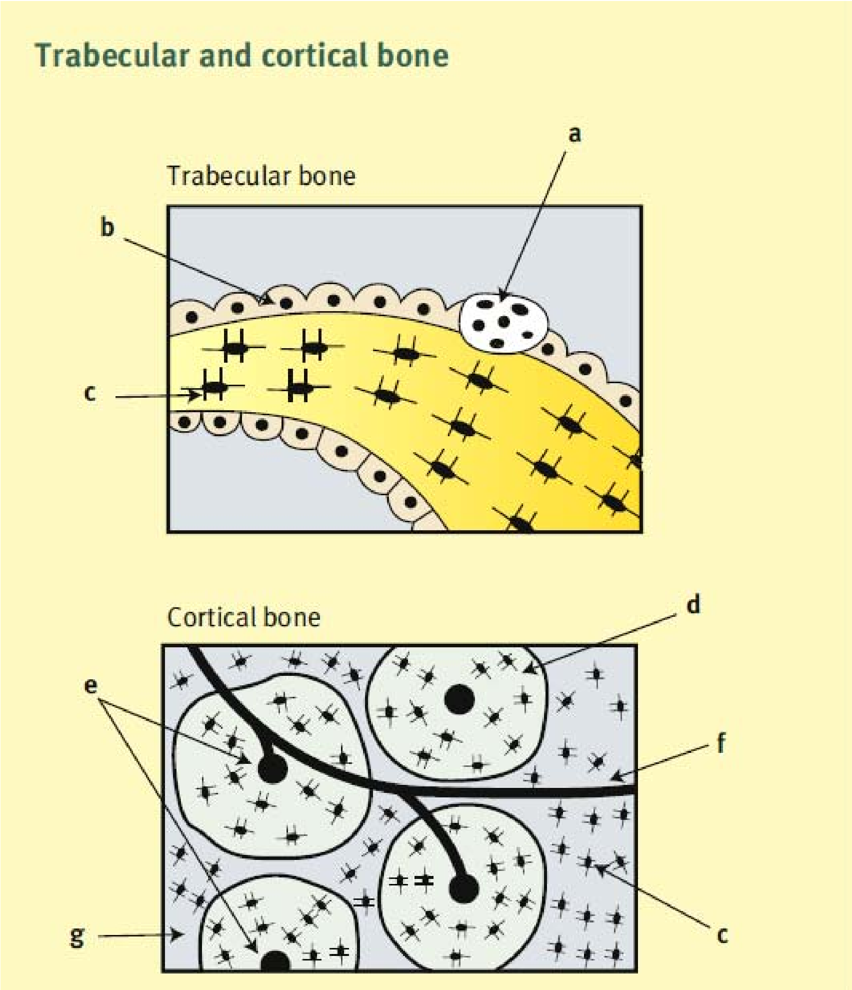

Figure 2.2

shows microscopic structure in cancellous and cortical bone.

a: osteoclast. **b**: osteoblast. **c**: osteocyte. **d**: concentric lamellae. **e**: capillaries in Haversian canal. **f**: capillary in Volkmann's canal. **g**: interstitial lamellae.

(Adapted from Little N, Rogers B and Flannery M, bone formation, remodelling and healing, basic science, elservier, 2011)

2.3.2 Bone healing

Bone healing (repair) can occur by different mechanisms dependent on both the mechanical and biological environments.

2.3.2.1 Primary (direct) bone healing

This occurs when there has been anatomical reduction of the fragments with direct cortical contact. Furthermore, there is interfragmentary compression and no movement between the fractures surfaces. This leads to absolute stability, popularized by Perren et al, 1979)

There is no callus formation and the bone heals by remodelling using BMUs and cutting cones (see Figure 2.3).Rigid plate fixation of fractures is an example of primary bone healing. If the gap between the fractured surfaces is too large then the BMUs may not be able to cross it and the fracture may not unite.

2.3.2.2 Secondary (indirect) bone healing

This occurs when there is movement at the fracture site and the bone heals via callus formation. There are several stages to indirect bone healing first described by Dupuytren in 1847.

2.3.3Stages of Bone Healing

Three main stages involve in bone healing :

2.3.3.1 Haematoma and inflammation (hours to days).

Bleeding from the bone and soft tissues leads to the formation of a haematoma and a fibrinous blood clot. This acts as a reservoir for the release of growth factors, and cytokines(IL-1, IL-6, transforming growth factor-b, bone morphogenetic proteins, platelet-derived growth factor, fibroblast growth factor and insulin-like growth factor). These stimulate angiogenesis to the area and migration of macrophages,PNMs, mesenchymal stem cells and fibroblasts. Haematoma is gradually replaced with fibrous tissue and the bone ends are resorped by osteoclasts.

2.3.3.2 Repair (see Figure 2.3).(within 2 weeks)

Primary callus occurs. Intramembranous bone forms at the periosteal layer. Type I collagen is laid down from primary osteoblasts found within the periosteal cambial layer, but does not bridge the fracture. Endochondral bone formation forms in the bridging callus. This joins the fracture ends and is produced by mesenchymal stem cells differentiating into chondroclasts and changing the fibrous network into a cartilaginous matrix(soft callus). This is calcified and invaded by blood vessels and osteoblasts which secrete osteoid. The cartilaginous matrix is changed into woven bone (hard callus).

2.3.3.3 Remodelling.

Woven bone is remodelled into hard lamellae bone by BMUs. It assumes a configuration based on the stresses applied to it (Wolff's law).

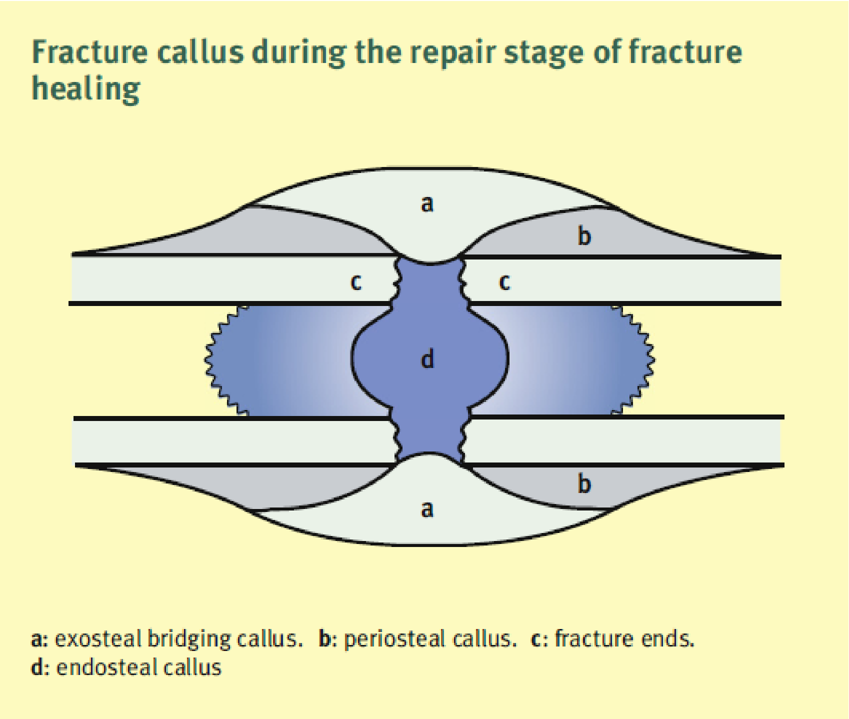

Figure 2.3 shows stages of bone healing (in bone repair stage):

a: exosteal bridging callus

b: periosteal callus

c: fracture ends

d: endosteal callus

(Adapted from Little N, Rogers B and Flannery M, bone formation, remodelling and healing, basic science, elservier, 2011)

2.3.4 Bone remodelling

2.3.4.1 Normal bone remodelling

Bone, being one of the largest organs in the body, plays a role in providing biomechanical support, allowing locomotion, haematopoiesis and calcium homeostasis.

Bone undergone substantial changes in structure, shape and composition according to the mechanical and physiological environment, an adaptive process known as bone remodelling. Bone adaptability allows for efficient repair. Ideally, bone formation matches bone resorption resulting in no net loss of bone mass.

Bone remodelling only occurs on the internal surfaces of the bone matrix (trabecular surfaces of cancellous bone and Haversian systems of cortical bone). Bone can only be added or removed by bone cells on these surfaces. This action is done by four types of bone cells, that is 1) Osteoblasts [OB] (produce bone), 2) Osteoclasts [OC](remove bone), 3) Bone lining cells (inactive osteoblasts that can be reactivated in response to chemical and/or mechanical stimuli) [Miller, 1992] and 4) osteocytes.

Bone remodelling occurs via basic multicellular units (BMUs),[Frost, 1963]. Each unit consists of a group of cells that remodel bone in response to a variety of biological and mechanical stimuli. BMUs are headed by OCs that act as cutting cones, removing trenches or tunnels of bone from the surfaces of trabecular and cortical bone (Boyce, 2008).These are followed by a capillary bed and a lining of OBs that fill in the trenches by laying down new bone matrix in them (Figure 2.4).

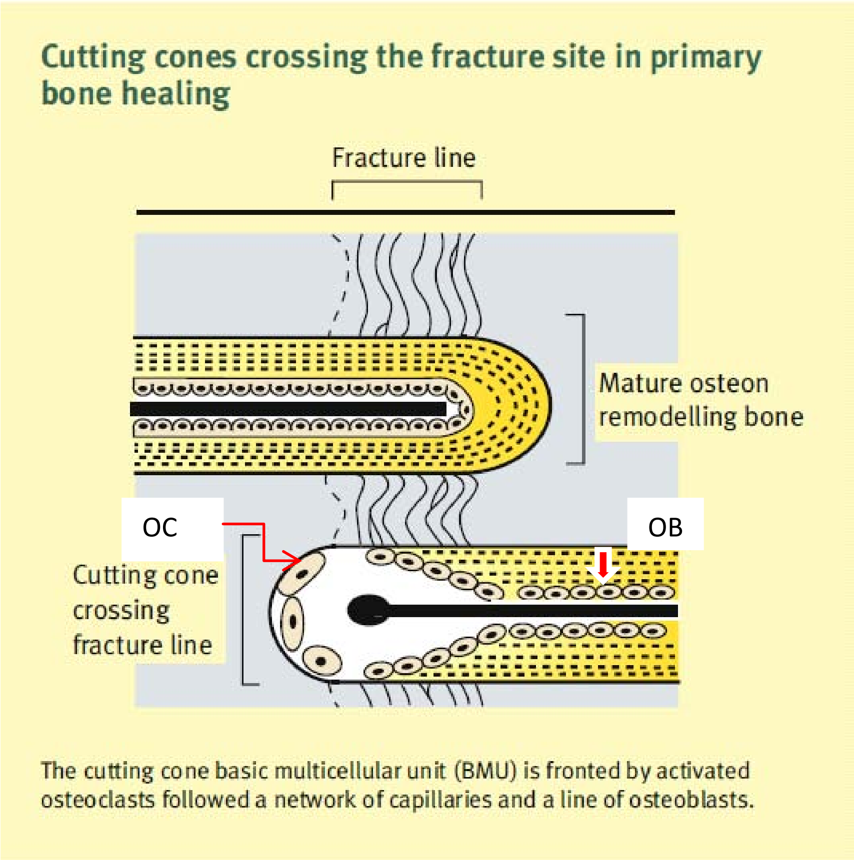

Figure2.4showsbone remodelling that occur via basic multicellular units (BMUs) in primary bone healing. OC : Osteoclasts, OB : Osteoblasts(Adapted from Little N, Rogers B and Flannery M, bone formation, remodelling and healing, basic science, Elservier, 2011)

2.3.4.2 Fracture Remodelling

Child periosteum has greater potential to form bone than that of adult. This add an extra stimulation to healing process, resulting in faster remodelling of fracture in children than in adults. Minimal deviations in alignment will be corrected faster, and even in gross deviations in alignment, excellent remodelling can occur.(Bilo et al, 2010).

Andrew et al stated that fracture healing in children demonstrate significant difference from that is seen in adult. The process of healing consists of the formation of hematoma followed by formation of granulation tissue mass. This include blood vessels and mesenchymal progenitor cells. These progenitor cells give rise to chondrocytes and osteoblast, generating bone either by endochondral or intramembranous ossification. The mass of new bone which is formed lies around the end of fractured bone rather than between them, and is known as the callus mass. Development of callus is faster in children than in adult, and generally, fracture is faster and more reliable in children (Mosely, 1992). Fracture healing in children, especially in those aged 10 years and younger, there is a rapid and extensive remodelling. Remodelling occurs by coupled osteoclasts and osteoblast removing and laying down bone. This result in the callus mass being completely remodelled over a period of 1-2 years, and eventually becoming almost undiscernible on X ray. This state is almost never attained in fracture of the cortex of adult long bones, although fracture cancellous bone may eventually become completely remodelled. The excellent remodelling in children's fracture is due to their faster rate of bone turnover, associated with the normal processes of growth.

2.3.5 Factors that influence fracture remodelling

2.3.5.1 Age

In normal bone remodelling, it prevents the occurrence of damage by adapting bone structure and hence bone strength to its loading circumstances. In bone remodelling, when damage inevitably occurs, bone removes the damage, in order to maintain bone strength. This cellular machinery is successful during growth, but fails during advancing age because of the development of a negative balance between the volumes of bone resorbed and formed during remodelling by the basic multicellular unit (BMU), high rates of remodelling during midlife in women and late in life in both sexes, and a decline in periosteal bone formation.(Martin ,2008).

In relation to age, there are at least four age-related changes in the cellular machinery of bone modelling and remodelling that compromise the material and structural properties of bone.(Seeman & Delmas,2006) The first age-related change in the cellular machinery is by Vedi (1982), whereby the author stated that remodelling rate is rapid during growth, because each remodelling event deposits only a small amount of bone(Parfitt, 2002).As growth nears its ‘programmed’ completion, rapid remodelling is no longer needed, and the remodelling rate slows. With the completion of longitudinal growth, the only requirement for bone formation is the repair of micro and macro-damage, so there is a decline in bone formation, a mechanism proposed to be responsible for bone fragility over 65 years ago (Albright, 1941).The mechanisms responsible for the reduction in the volume of bone formed in each BMU may include a reduction in stem-cell precursors of osteoblasts, a reduction in differentiation of stem cells to the osteoblast lineage (as adipocytogenesis is favoured), reduced osteoid production of individual cells, and a reduction in the life span of these cells(Bonyadi, 2003).

The second abnormality in remodelling is believed to be an increase in the volume of bone resorbed by the BMU, but this may be confined to a brief period following sex hormone deficiency (Manolagas, 2000).The opposite may occur through life, whereby the volume of bone resorbed by each BMU appears to decrease as reflected in a lower resorption cavity depth and an age-related increase, rather than decrease, in interstitial thickness(Eriksen, 1999).

The third age-related abnormality in the cellular machinery contributing to structural decay is an increase in the rate of bone remodelling after menopause. This is accompanied by worsening of the negative bone balance in each BMU as the volume of bone resorbed increases and the volume of bone formed decreases, study done by Manolagas, 2000.

The fourth age-related changes in the cellular machinery is also a reduction in bone formation at the tissue level;bone modelling on the periosteal envelope slows after completion of longitudinal growth, but continues slowly, so that bone diameters enlarge, but by no more than a few millimetres during the next 60 years(Szulz, 2006).This is insufficient to compensate for vigorous endosteal bone loss from the endocortical surface (producing cortical thinning), from the intracortical surface (producing intracortical porosity), and from the trabecular surface (producing trabecular thinning), and hence complete loss of trabeculae and loss of connectivity. Based on these four age-related changes in the cellular machinery of bone modelling and remodelling, it can be concluded that age plays a major role in bone remodelling, thus the older the age of the patient, the less bone remodelling that can occur.

Remodelling of fracture in different age group differs in:

1) Young person

As stated before, child periosteum has greater potential to form bone than that of adult. This add an extra stimulation to healing process, resulting in faster remodelling of fracture in children than in adults. Minimal deviations in alignment will be corrected faster, and even in gross deviations in alignment, excellent remodelling can occur.(Bilo et al, 2010).

Stilli et al (2007) also emphasized that bone in children is characterised by a greater flexibility, by a porosity greater than in adult bone and by a periosteum that is much thicker than in the matureskeleton and loosely attached to the shaft bone (whereas it is densely attached to the physis), and has a richer vascularisation. Furthermore, in children, the bone has a greater capacity for fracture healing, by expression of a strong osteogenic potential, which is inversely proportional to age.

Study by Reynolds (1981) showed that there is an increase in the rate of growth in fracture femur especially if there is an overlap of fracture edges due to natural process of fracture remodelling in children.

2) Old person.

There are differences in fracture remodelling in older patient. This can be explained by few studies by certain author.

O'Driscoll et al , 2001 stated that there is thinning of cambium layer as a person becoming older, thus this diminish the ability of the cartilage, and likely also bone formation.

Brandes et al, 2005 also stated that there is alterations in the structural and regulatory components of the matrix contiguous to form vessels

(angiogenesis) in aged tissue that could influence the bone healing in elderly patients.

Factors impairing fracture healing may include the limited capacity of the elderly to neutralize reactive oxygen species of the respiratory chain. Free radicals produced by the respiratory chain may cause oxidative damage to various cellular components which may affect cellular function, also involving cells of osteogenic and chondrogenic lineage (Carrington et al, 2005)

2.3.5.2. Site of fracture

The rate of remodeling differs with the location of the fracture site.

Metaphysis: The metaphysis serves as an active remodeling area in the development of normal bone growth. This is where the quantity of woven bone produced in the adjacent physis is replaced with the more structurally sound quality compact bone of the diaphysis. Thus, this area already has in place an increased vascularity with much more osteogenic potential to facilitate fracture healing. The osteogenesis in this area is normally active.

Diaphysis: The diaphysis is an area in which there is relatively dormant osteogenesis. The bone production in this diaphyseal region is a balance of subperiosteal intramembranous ossification on the surface coupled with endosteal bone reabsorption in the medullary canal. The bone here is rigid, compact cortical bone and thus relatively avascular. As a result, there is less remodeling potential in this area. Fractures in this area take longer to heal and remodel.

Study done by Schnitzer et al (1982) by using dogs to quantify the chondro-osseous circulation, the author found out that blood flow to the metaphyseal region of femur in this canine is 50 to 100% more than the blood flow to the femoral diaphysis. This also explain why metaphysis remodelled better compared to diaphysis.

McKinstry et al (1982) measured the uptake off $_{99}$TC-MDP injected intravenously into immature and mature dogs (uptake depending on blood flow) . Apart from finding out that the uptake increased following osteotomy, the author found out that highest arterial blood flow was in the metaphyseal region (1.5mm immediately under the physis).

Stilli et al (2006) found out that fracture that located near the growth plate (metaphyseal region) remodelled more than diaphyseal fractures.

2.3.5.3 Remodelling in plane of angulation

Physis: Wallace et al, 1992, stated that in the skeletally immature individual, 75% of the angular remodeling takes place in the physis. Pauwels (1975), Ryoppy, and Karaharju (1974) have demonstrated that physes adjacent to a fracture tend to realign to become perpendicular to the forces acting through them by a process of asymmetrical growth. The concave side grows more rapidly to align the physis so as to become perpendicular to the long axis of the shaft of the bone. Once the physis is realigned, it then resumes symmetrical growth.

Diaphysis: In the diaphysis, remodeling follows Wolf's law (1892). Here, concave side has increased pressure (compression) on that side that stimulates new bone formation. On the convex side, the bone is under tension and undergo reabsorption of the convexity. About 20% of the remodelling of the angulation occurs in this area.

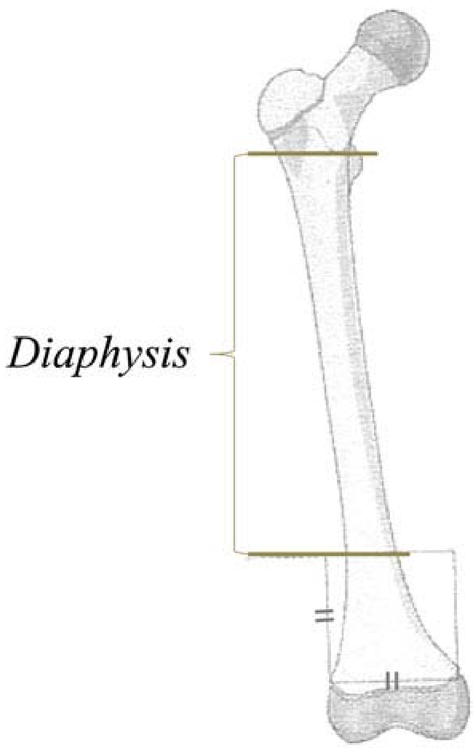

Figure 2.5 shows location of diaphysis.

(Adaptedfrom Kamegaya M, Saisu T,Segawa Y, Remodeling of angulation deformities in diaphyseal femoral fracture in children, The Japanese Orthopaedic Association 2012)

Reynolds (1981) studied 42 fractures of shaft of femur in children (age 13 and less) to determine effects of the injury to the growth of femur (remodelling). Apart from the result that the author obtained regarding 85% remodelling of fracture already occur within 2 years, 5 out of 42 fractures femur (12%), achieved less correction of angulation. (degree of angulation was not stated in this study).

Study done by Stilli in 2006 , 1162 femoral fracture patient was recruited (treated conservatively), author recorded greater remodelling occur in sagittal compare to coronal plane, with remodelling occur more in children less than 8 years old.

Kamegaya et al did a study in 2012, whereby they recruited 39 patients who has residual angulation deformity > 5˚ at femur fracture site (diaphyseal region). The author follow them up with average of 30.4 months. Their aim is to know the remodelling of angulation deformities for diaphyseal femoral fracture in children. They concluded that remodelling occur on the coronal plane (varus and valgus) rather than on the sagittal plane (flexion and extension) in patient age 0 to 5 years and equally on both planes from the age 6 to 9 years and more than 10 years old.The average correction rate is significantly higher (coronal plane) in the younger age group (67 % will remodelled) and as the child age gets older (more than 10 years old), the remodelling become less (only 18.2 % will remodelled). They also found out that the correction of deformity is more on the proximal one third (47.8 % remodelled) in coronal plane.

2.3.5.4 Hormones

Activated osteoblasts stimulate osteoclasts to resorb bone via the RANK-RANK-L pathway. OBs produce RANK-L (also known as osteoclast differentiation factor) in response to PTHrP, vitamin prostaglandin E2 (PGE2), interleukins 1 and 2 (IL1 and IL2). RANK-L binds to a receptor (RANK) on immature osteoclasts to stimulate osteoclastic differentiation and osteoclastic bone resorption (see Figure 2.6). OBs also produce osteoprotegerin (OPG) which acts as a decoy receptor for RANK-L therefore limiting osteoclastic differentiation.However, regulation of the complex autocrine, paracrine and endocrine pathways are still not fully understood.

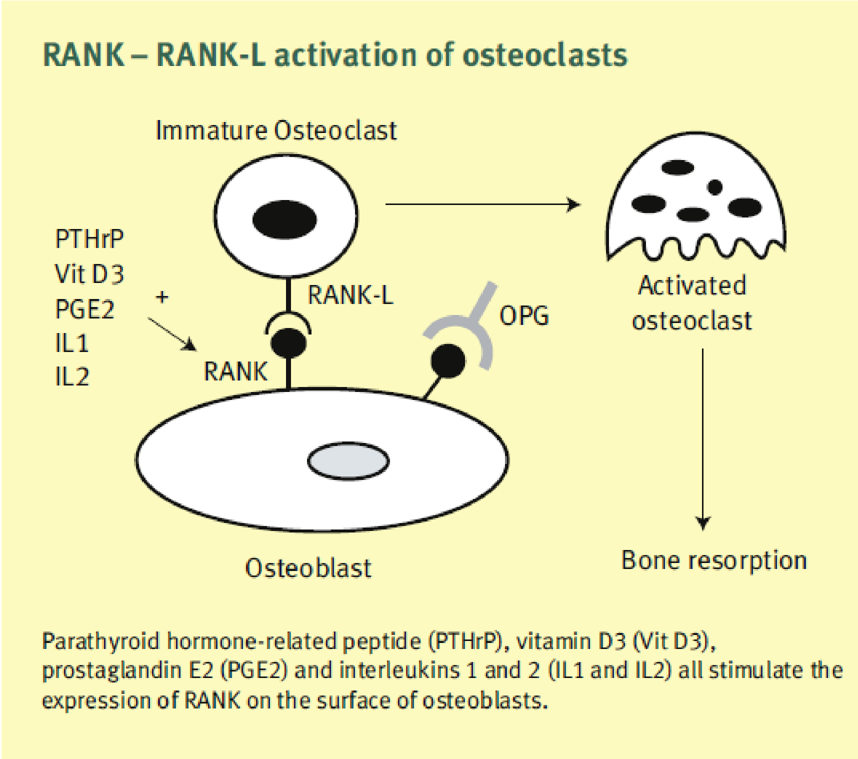

Figure 2.6 : Hormones that influenced activation of osteoclasts

(Adapted from Little N, Rogers B and Flannery M, bone formation, remodelling and healing, basic science, elservier, 2011)

In regards to parathyroid hormone-related protein (PTHrP), it is a paracrine regulator which signals through the receptor it shares with PTH expressed in the osteoblast. PTHrP is important for the commitment of precursor cells to the osteogenic lineage and subsequent maturation.PTHrP stimulates bone formation by enhancingosteoblast differentiation, and reduces osteoblast apoptosis. These effects require short-lived, high levels of PTHrP locally to favour bone formation. Persistently increased local PTHrP favours osteoclast