The Thai Journal of Orthopaedic Surgery

The Official Journal of the Royal College of Orthopaedic Surgeons of Thailand

ISSN 0125-7552

Volume 37 / Number 1-4 January-October 2013

The Thai Journal *Of* Orthopaedic Surgery

The Official Journal of the Royal College of Orthopaedic Surgeons of Thailand

ISSN 0125-7552

Volume 37 / Number 1 January 2013

The Council Members of the Royal College of Orthopaedic Surgeons of Thailand (RCOST) 2012-2014

President	**Thavat Prasartritha, MD**
Immediate Past President	**Adisorn Patradul, MD**
President Elect	**Sukit Saengnipanthkul, MD**
1st Vice-President	**Banchong Mahaisavariya, MD**
2nd Vice-President	**Aree Tanavalee, MD**
Registrar	**Chumroonkiet Leelasestaporn, MD**
Treasurer	**Thawee Songpatanasilp, MD**
Secretary General	**Keerati Chareancholvanich, MD**
Assistant Secretary General	**Charlee Sumettavanich, MD**
Promotion	**Thana Turajane, MD**
Council Members	**Sumroeng Neti, MD**
	Pijaya Nagavajara, MD.
	Kanyika Chanmiprasas, MD
	Preecha Chalidapong, MD
	Warat Tassanawipas, MD
	Chiroj Sooraphanth, MD
	Thipachart Bunyaratabandhu, MD
Advisory Board	**Samak Bukkanasen, MD**
	Natee Rukpollamuang, MD
	Direk Israngkul, MD
	Suprija Mokkhavesa, MD
	Charoen Chotigavanich, MD
	Vinai Parkpian, MD
	Pongsak Vathana, MD
	Prasit Gonggetyai, MD
	Chaithavat Ngarmukos, MD
	Thamrongrat Keokarn, MD
	Suthorn Bavonratanavech, MD
	Wichien Laohacharoensombat, MD
	Saranatra Waikakul, MD

the 35th Annual Meeting of RCOST 2013
Pattaya, Chonburi Province, Thailand on October 20-22, 2013

ราชวิทยาลัยแพทย์ออร์โธปิดิกส์แห่งประเทศไทย

The Royal College of Orthopaedic Surgeons of Thailand

ขอเรียนเชิญแพทย์และผู้สนใจเข้าร่วมฟังการบรรยาย

วันอาทิตย์ที่ 20 ตุลาคม 2556 เวลา 11.30-13.00 น.

Interactive workshop:

งานวิจัยสำหรับการขอกำหนดตำแหน่งนายแพทย์เชี่ยวชาญ

11.30 - 11.40 ปัญหาหนักใจใน ซี 9

11.40 - 12.00 ช่วยอย่างไร...ทำไมไม่ได้
กรรมการ Research Section

12.00 - 12.40 เสวนา...ปริศนาคาใจ
กรรมการผู้ประเมินและผู้เข้าร่วมประชุม

12.40 - 13.00 ราชวิทยาลัยจะทำอย่างไรดี
กรรมการราชวิทยาลัย

The Thai Journal of Orthopaedic Surgery

Past Editorial Board (2012-2013)

Editorial office address: The Royal College of Orthopaedic Surgeons of Thailand
4 th Floor, Royal Golden Jubilee Building, 2 Soi Soonvijai, New Petchburi Road, Bangkapi, Huay Khwang, Bangkok 10310
E-mail: secretariat@rcost.or.th, supawineep@rcost.or.th
Telephone: +66 2 7165436-7
The Journal is free online at http://www.rcost.or.th, http://thailand.digitaljournals.org/index.php/JRCOST

the 35th Annual Meeting of RCOST 2013
Pattaya, Chonburi Province, Thailand on October 20-22, 2013

ราชวิทยาลัยแพทย์ออร์โธปิดิกส์แห่งประเทศไทย

The Royal College of Orthopaedic Surgeons of Thailand

ขอเรียนเชิญแพทย์และผู้สนใจเข้าร่วมฟังการบรรยาย

วันจันทร์ที่ 21 ตุลาคม 2556

RCOST Symposia 1: <u>Ethics & law in orthopaedic practice</u>

- แนวโน้มปัญหาจริยธรรมในวิชาชีพออร์โธปิดิกส์ ศ.นพ. สุกิจ แสงนิพันธ์กูล

- กรณีศึกษาทางจริยธรรมและมาตรฐานวิชาชีพ นพ. ต่อพล วัฒนา

- การเตรียมตัว เมื่อเกิดปัญหาที่อาจถูกฟ้องร้อง นพ. วันชัย ศิริเสรีวรรณ

RCOST Symposia 2: <u>Meet the Jedi Episode II</u>

- นพ. พงษ์ศักดิ์ วัฒนา

- นพ. สุปรีชา โมกขะเวส

- นพ. ก่อกู้ เชียงทอง

RCOST Symposia 3: <u>Tips & pitfalls in researches & publications</u>

<u>(สำหรับการขอตำแหน่งนายแพทย์เชี่ยวชาญ)</u>

Moderator : นพ. วิวัฒน์ สุรางค์ศรีรัฐ

Panelists:

- ศ.เกียรติคุณ นพ. เจริญ โชติกวณิชย์

- รศ.นพ. วินัย พากเพียร

- นพ. ยิ่งยง สุขเสถียร

- นพ. พลวรรธน์ วิทูรกลชิต

RCOST Symposia 4: <u>การเบิกจ่ายวัสดุอุปกรณ์ทางการแพทย์ของ 2 กองทุน</u>

Moderator : นพ.ชาลี สุเมธวาณิชย์

- นพ. การุณย์ คุณติรานนท์ (สปสช)

- คุณ อภิสมา ชาญสืบกุล (กรมบัญชีกลาง)

The Thai Journal of Orthopaedic Surgery Volume 37 Number 1 January 2013

Contents

สารบัญ

นิพนธ์ต้นฉบับ หน้า

Anatomy of the Cruciate Ligaments of the Knee Joint in a Thai Population

Prasit Wongtriratanachai, MD, Nopporn Niwattananun, MD, Sattaya Rojanasathien, MD

Department of Orthopaedics, Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand

Purpose: *To study the anatomy of the anterior cruciate and posterior cruciate ligaments.*
Methods: *Twenty-two Thai cadaveric knees without previous surgery were used for anatomical study of the ACL and the PCL for size and location.*
Results: *The anterior cruciate ligament had an average length of 33.1 millimeters, and an average width of 10.0 millimeters. The posterior cruciate ligament had an average length of 33.0 millimeters, and an average width of 11.0 millimeters. By using the Wilcoxon rank sum and sign rank tests, no difference was found between gender, sides, and length (P>0.05). We did find that the middle portion of the posterior cruciate ligament was statistically wider than that of the anterior cruciate ligament (P<0.05). The axis of the femoral attachment of the anterior cruciate ligament tilted forward to the vertical axis an average of 26.3 degrees. The average width of the attachment to the femur and the tibia was 16.3 millimeters and 20.0 millimeters, respectively. The attachment of ACL at femur is more posterior and at tibia is more anterior in Thai population. The posterior cruciate ligament was attached to the anterior part of the lateral surface of the medial femoral condyle. The axis of the attachment aligned with the horizontal. The average widths of the femoral and tibial attachment were 19.7 millimeters and 13.9 millimeters, respectively.*
Conclusion: *Clinical application of these findings to aid in the location of the attachment site of a tendon graft in the surgical treatment of chronic knee instability will benefit Thai patients.*

Keywords: *Anatomy, cruciate, ligament, knee, Thai*

The Thai Journal of Orthopaedic Surgery: 37 No.1: 1-7
Full text. e journal: *http://www.rcost.or.th, http://thailand.digitaljournals.org/index.php/JRCOST*

Introduction

Cruciate ligaments of the knee create most of the problems of chronic knee instability in all age groups. Major causes of injury are sports and traffic accidents. Anterior cruciate ligament(ACL) and posterior cruciate ligament(PCL) were the most common ligament injury in the knee joint[1], and an operation is acceptable for a patient who suffers from knee instability. One preferable operation nowadays is intraarticular reconstruction using bone-patella tendon-bone[2-7], or a tendon from the medial hamstring[8-11] which has equal or greater strength and does not compress the nearby structures: posterior cruciate ligament and intercondylar notch. The most critical factors in obtaining a successful operation is proper graft placement[12-14], so size and attachment location of the ACL and the PCL should be basic knowledge for bone surgeons.

The anatomy of the ACL and the PCL in a Thai population has not as yet been reported, hence our interest in this study for the following purposes:

1. anatomical study of the ACL and the PCL for size and location on the femur and the tibia;
2. comparison with previous studies in non-Thai populations;
3. clinical applications in ligament reconstruction; and
4. preparation for a further study to guide the size of a tendon graft in knee ligament reconstruction in a Thai population

Correspondence to: Wongtriratanachai P, Department of Orthopaedics, Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand
E-mail: prasitjo@gmail.com

Materials and Methods

We studied the anatomy of 22 cadaveric knees provided by the Department of Anatomy, Faculty of Medicine, Chiang Mai University. Six male (12 knees) and 5 female cadavers (10 knees), with an age range from 25 to 82 years (average 56.5 years) were included. None had a history of knee trauma or knee surgery. The anatomy of the ACL and the PCL was studied as follows:

1. the tibia was cut 15 centimeters below the knee, and the femur 15 centimeters above;
2. the skin, muscle, vessels and synovial tissue was then dissected from the knee joint;
3. an oscillating saw was used to divide the femoral bone in the sagittal plane to view the origins of the ACL and the PCL;
4. the length and width of each ACL and PCL was measured; and
5. all ACL and PCL were cut at the bony attachment to measure the relationship between the

attachment site and bony structure (see figures 1 and 2).

A vernier caliper was used for length measurement and a goniometer for angle measurement. Each measurement was repeated three times and the mean calculated.

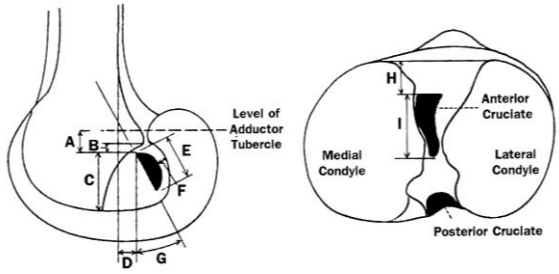


Fig. 1 Attachment site of anterior cruciate ligament and bony landmarks
A: distance between the most superior femoral attachment and the level of the adductor tubercle
B: distance between the most superior femoral attachment and the roof of posterior intercondylar notch
C: distance between the most superior femoral attachment and the border of the distal articular cartilage
D: distance between the most anterior femoral attachment and the axis of posterior femoral cortex
E: Length of the femoral attachment site
F: distance between the posterior femoral attachment and the border of the posterior articular cartilage
G: Angle between the axis of the attachment and the vertical axis
H: distance between the anterior edge of tibia articular surface and the most anterior tibial attachment
I: Length of the tibial attachment site

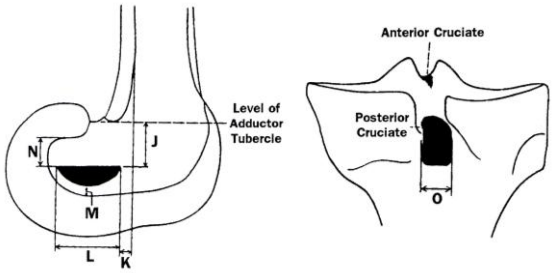


Fig. 2 Attachment sites of posterior cruciate ligament and bony landmarks
J: distance between the most superior attachment and a level of adductor tubercle
K: distance between the most anterior femoral attachment and the axis of posterior femoral cortex
L: Length of the femoral attachment site
M: distance between the most distal femoral attachment and the border of the distal articular cartilage
N: distance between the most superior femoral attachment and the roof of posterior intercondylar notch
O: Width of the tibial attachment site

Statistical analysis

1. Data was calculated for a mean and a standard deviation for a size and a distance between the bony structures, and separated for right and left knee and for male and female.

2. Wilcoxon rank sum test (Mann Whitney U test) was used for comparison between right and left knees and between males and females.

3. Wilcoxon sign rank test was used for comparison between ACL and PCL in the same knee.

Results

Anterior Cruciate Ligament

1. Dimensions

ACL: length from 30.5 to 38.7 millimeters (average 33.1 millimeters). There was a standard deviation of 1.8 millimeters and Mean ± SD 31.3-34.9 millimeters (table 1).

ACL: width from 8.1-12.1 millimeters (average 10.0 millimeters). There was a standard deviation 1.1 millimeters and Mean ± SD 8.9-11.1 millimeters (table 1).

There was no statistical significance between male and female, or between right and left knees in length and width of ACL ($p>0.05$) (table 1).

Table 1 Average length and width at mid portion of ACL in Thai population

Sample	Length (millimeter)			Width at mid portion (millimeter)		
	Range	Mean	SD	Range	Mean	SD
All samples (n=22)	30.5-38.7	33.1	1.8	8.1-12.1	10.0	1.1
By side						
Right knee (n=11)	31.2-35.8	33.0	1.4	8.1-12.1	10.0	1.2
Left knee (n=11)	30.5-38.7	33.2	2.2	8.4-12.0	10.0	1.0
By gender						
Right knee (n=12)	30.5-38.7	33.2	2.3	8.1-12.1	9.9	1.3
Left knee (n=10)	31.7-34.1	32.9	0.8	9.1-11.3	10.1	0.7

2. Femoral attachment

ACL was attached to the posterior aspect of the medial surface of the lateral femoral condyle and the attachment site was semicircular. The axis of the femoral attachment tilted forward to the vertical axis and the relationship with the bony structure is shown in table 2.

3. Tibial attachment

ACL was attached laterally to the anterior tibial spine. A distance from the anterior edge of tibial articular surface to the most anterior tibial attachment (H) ranged from 10.2-14.4 millimeters (average 12.7 millimeters). The length of the ACL tibial attachment (I) ranged from 15.0-22.8 millimeters (average 20.0 millimeters), (table 2).

Table 2 Distance between the attachment site of ACL (n=22) and the bony landmark in Thai population

Parameters	Range	Mean	SD	Mean ± SD
A	4.2-9.0	6.0	1.6	4.4-7.6
B	0.9-8.3	3.7	2.3	1.4-6.0
C	14.1-18.9	15.8	1.4	14.4-17.2
D	13.3-20.8	16.8	2.6	14.2-19.4
E	12.1-18.5	16.3	1.6	14.7-17.9
F	0.0-4.1	1.4	1.4	0.0-2.8
G	19-38	26.3	6.2	20.1-32.5
H	10.2-14.4	12.7	1.2	11.5-13.9
I	15.0-22.8	20.0	2.1	17.9-22.1

Table 3 Average length and width at mid portion of PCL in Thai population

Sample	Length (millimeter)			Width at mid portion (millimeter)		
	Range	Mean	SD	Range	Mean	SD
All samples (n=22)	29.4-38.1	33.0	2.5	9.8-13.0	11.0	0.8
By side						
Right knee (n=11)	29.4-38.1	32.9	2.7	10.0	13.0	1.1
Left knee (n=11)	29.7-36.5	33.0	2.3	9.8-12.1	10.9	0.8
By gender						
Right knee (n=12)	29.4-38.1	32.7	3.2	10.2-13.0	11.4	0.8
Left knee (n=10)	32.0-35.0	33.3	1.1	9.8-11.7	10.5	0.6

Posterior Cruciate Ligament

1. Dimensions

PCL: length from 29.4 to 38.1 millimeters (average 33.0 millimeters). There was a standard deviation of 2.5 millimeters and Mean ± SD 30.5-35.5 millimeters (table 3).

PCL: width from 9.8-13.0 millimeters (average 11.0 millimeters). There was a standard deviation 0.8 millimeter and Mean ± SD 10.2-11.8 millimeters (table 3).

There was no statistical significance comparing between male and female, or between right and left knee in length and width of PCL ($p>0.05$) (table 3).

2. Femoral attachment

The PCL was attached on the anterior of lateral surface of medial femoral condyle and the attachment site was semicircular shape similar to the ACL. The axis of the femoral attachment paralleled to the horizontal axis and the relationship with the bony structure was shown in table 4.

3. Tibial attachment

The PCL was attached at the posterior edge of tibia and the width (O) was ranged from 11.1 to 18.7 millimeters (average 13.9 millimeters). There was a standard deviation 2.1 millimeters and Mean ± SD 11.8-16.0 millimeters (table 4).

Table 4 Average distance between the attachment site of PCL (n=22) and the bony landmark in Thai population

Parameters	Range	Mean	SD	Mean ± SD
J	7.5-21.8	15.6	4.1	11.5-19.7
K	0.0-11.2	6.5	3.6	2.9-10.1
L	16.0-27.4	19.7	3.6	16.1-23.3
M	0.0-5.2	1.0	1.6	(-0.6)-2.6
N	7.2-17.9	12.9	2.8	10.1-15.7
O	11.1-18.7	13.9	2.1	11.8-16.0

The relationship between ACL and PCL

In the same knee, there was no statistical significance in comparison of the length of the ACL and the PCL ($P>0.05$), but at the mid portion of the tendons, the width of the PCL was larger than the ACL (statistically significant, $P<0.05$).

Discussion

The operative treatment in the patient with knee instability from anterior cruciate ligament injury has been reported by many authors[2-11]. The most popular procedure is an intraarticular procedure which provides similar biomechanics to the natural ACL, more so than provided by extraarticular procedures[14]. A bone-patella tendon-bone graft (BPTB) is one of the most popular tissues for a ligament reconstruction because it provides good strength compared to other grafts[15]. However, good treatment results depend on many factors such as graft fixation, graft tension, and notchplasty but the most important factor is the anatomical location of the graft[12-14], especially the femoral attachment site of the reconstructed tendon. If the graft is placed more anteriorly, it is too tight in flexion and too loose in extension. Conversely, a graft placed more posteriorly would produce looseness in flexion and tightness in extension. Thus the patient cannot perform full knee extension, lacks stability, and may suffer from many complications.

Reconstruction procedures require knowledge of the basic anatomy of the ACL and the PCL. No previous study has been reported yet in Thailand. Previous data from international journals may not apply clinically in a Thai population. Hence the authors decided to undertake the present research to establish Thai reference data for these two ligaments.

Anterior Cruciate Ligament

According to our study, the average width of the Thai ACL at the mid portion is 10.0 millimeters and average length 33.1 millimeters. This is less than found in the study by Girrgis FG[16], in which the ACL had an average width of 11.0 millimeters and an average length of 38.0 millimeters (table 5). A difference of a distance of the attached location on a bony structure was shown in table 6.

Data that must be known in order to perform an operation of anterior cruciate ligament reconstruction are:

1. the distance between the most superior femoral attachment and the roof of posterior intercondylar notch (B) in a Thai population is 3.7 millimeters;
2. the length of the femoral attachment site (E) in Thai population is 16.3 millimeters;
3. the distance between the posterior femoral attachment and the border of the posterior articular cartilage (F) in Thai population is 1.4 millimeters.

Posterior Cruciate Ligament

According to our study, PCL had the average width at the mid portion of 11.0 millimeters, and an average length of 33.0 millimeters which were less than the study from Girgis FG[16], where the PCL had the average width 13.0 millimeters and average length 38.0 millimeters (table 5). Difference in the distance of the attachment location on a bony structure are shown in table 7.

Data that must be known in order to perform an operation of posterior cruciate ligament reconstruction are

1. length of the femoral attachment site (L) in Thai population is 19.7 millimeters; and
2. distance between the most distal femoral attachment and the border of the distal articular cartilage (M) in Thai population is 1.0 millimeter

Table 5 Average dimensions of ACL and PCL as compared to another study

Study	Anterior Cruciate Ligament		Posterior Cruciate Ligament	
	Length	Width	Length	Width
Girgis FG[16]	38.0	11.0	38.0	13.0
Chiang Mai	33.1	10.0	33.0	11.0

Table 6 An average distance between the attachment site of ACL and the bony landmark

Study	Anterior Cruciate Ligament								
	A	B	C	D	E	F	G	H	I
Girgis FG[16]	12	4	12-20	8	23	4	25	15	30
Chiang Mai	6.0	3.7	15.8	16.8	16.3	1.4	26.3	12.7	20.0

Table 7 An average distance between the attachment site of PCL and the bony landmark

Study	Posterior Cruciate Ligament					
	J	K	L	M	N	O
Girgis FG[16]	23	5	32	3	15	13
Chiang Mai	15.6	6.5	19.7	1.0	12.9	13.9

Brantigan OC[17] and Palmer I[18] concluded that the PCL was shorter than the ACL, but our study has shown that the length of the two ligaments is similar in the same knee, with no statistical significance (P>0.05) for the two ligaments similarly to study of Girgis FG[16].

The limitation of this study is small sample size which perhaps does not reflect the whole Thai population. The data from our study have shown that the width and length of the Thai ACL and PCL are less than the measurements reported in many international reports. This may be caused by the smaller stature of Thai people when compared to Europeans. It is interesting to note that the proper width of a graft for ligament reconstruction in a Thai population should less than that which would be used in European people[2-7]. The lower width of the graft (10millimeters) could reduce the complication of graft compression between the intercondylar notch and the PCL. The smaller width may also reduce complications at the donor site. This requires further study to verify the the proper graft size for Thais requiring knee reconstruction.

Compared to the study of Girgis FG[16], the anatomy of ACL and PCL in a Thai population is shown in figure 3. For ACL reconstruction, the attachment at femur is more posterior and at tibia is more anterior in Thai population, so the reference attachment from the study of Girgis FG can cause too anterior at femur and too posterior at tibia for Thai population. For PCL reconstruction, the attachment at femur and tibia is similar from Thai population and from study of Girgis FG.

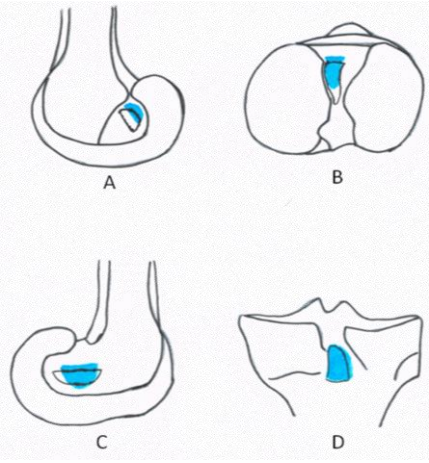


Fig. 3 The anatomy of ACL (A and B) and PCL (C and D) in Thai population (blue) compared to the study of Girgis FG[16] (black).

Conclusion

The results of this study have demonstrated the anatomy of the ACL and the PCL in Thais. This should be considered basic data for the Orthopedist when treating the patient with knee instability due to ligaments injury. Often we cannot clearly identify the attachment site of the ligaments, so we may use these data to point to the proper attachment of the tendon graft using bony structures as a reference. Finally, these data will help the investigator to study further how to select the best location for a tendon graft in knee ligament reconstruction.

Acknowledgements

We would like to thank Department of Anatomy, Faculty of Medicine, Chiang Mai University for cadaveric support of this study.

References

1. Miyasaka KC, Daniel DM, Stone ML, Hirschman P. The incidence of knee ligament injuries in the general population. Am J Knee Surg 1991; 4: 3-8.
2. Clancy WG, Jr., Nelson DA, Reider B, Narechania RG. Anterior cruciate ligament reconstruction using one-third of the patellar ligament, augmented by extra-articular tendon transfers. J Bone Joint Surg Am 1982; 64: 352-9.
3. Engebretsen L, Benum P, Fasting O, Molster A, Strand T. A prospective, randomized study of three surgical techniques for treatment of acute ruptures of the anterior cruciate ligament. Am J Sports Med 1990; 18: 585-90.
4. Shelbourne KD, Whitaker HJ, McCarroll JR, Rettig AC, Hirschman LD. Anterior cruciate ligament injury: evaluation of intraarticular reconstruction of acute tears without repair. Two to seven year followup of 155 athletes. Am J Sports Med 1990; 18: 484-8; discussion 8-9.
5. O'Brien SJ, Warren RF, Pavlov H, Panariello R, Wickiewicz TL. Reconstruction of the chronically insufficient anterior cruciate ligament with the central third of the patellar ligament. J Bone Joint Surg Am 1991; 73: 278-86.
6 Eriksson E. Reconstruction of the anterior cruciate ligament. Orthop Clin North Am 1976; 7: 167-79.
7. Marshall JL, Warren RF, Wickiewicz TL, Reider B. The anterior cruciate ligament: a

technique of repair and reconstruction. Clin Orthop Relat Res 1979; 143: 97-106.
8. Lipscomb AB, Johnston RK, Snyder RB. The technique of cruciate ligament reconstruction. Am J Sports Med 1981; 9: 77-81.
9. Puddu G. Method for reconstruction of the anterior cruciate ligament using the semitendinosus tendon. Am J Sports Med 1980; 8: 402-4.
10. Zaricznyj B. Reconstruction of the anterior cruciate ligament using free tendon graft. Am J Sports Med 1983; 11: 164-76.
11. Zarins B, Rowe CR. Combined anterior cruciate-ligament reconstruction using semitendinosus tendon and iliotibial tract. J Bone Joint Surg Am 1986; 68: 160-77.
12. Robert H, Miller III. Knee injuries. In: Canale S, editor. Campbell's operative orthopaedics. 9th ed. St.Louis: Mosby; 1998. p. 1113-300.
13. Shelbourne KD, Patel DV. ACL reconstruction using the autogenous bone-patellar tendon-bone graft: open two-incision technique. Instr Course Lect 1996; 45: 245-52.
14. Keneth L, Lambert, Cunningham RR. Anatomic substitution of the ruptured ACL using a vascularized patellar tendon graft with interference fit fixation. In: Feagin J, editor. The crucial ligament. New York: Churchill Livingstone; 1988. p. 401-8.
15. Noyes FR, Butler DL, Paulos LE, Grood ES. Intra-articular cruciate reconstruction. I: Perspectives on graft strength, vascularization, and immediate motion after replacement. Clin Orthop Relat Res 1983; 172: 71-7.
16. Girgis FG, Marshall JL, Monajem A. The cruciate ligaments of the knee joint. Anatomical, functional and experimental analysis. Clin Orthop Relat Res 1975; 106: 216-31.
17. Brantigan OC, Voshell AF. The mechanics of the ligaments and menisci of the knee joint. J Bone Joint Surg Am 1941; 23: 44-66.
18. Palmer I. On the injuries to the ligaments of the knee joint: A clinical study. Acta Chir Scand 1938; 81: 2-282.

กายวิภาคของเอ็นไขว้ในข้อเข่าในคนไทย

ประสิทธิ์ วงศ์ตรีรัตนชัย, พบ, นพพร นิวัฒนนันท์, พบ, สัตยา โรจนเสถียร, พบ

วัตถุประสงค์*: เพื่อศึกษากายวิภาคของ Anterior cruciate ligament (ACL) และ Posterior cruciate ligament (PCL) ในแง่ของขนาดและตำแหน่งในคนไทย*

วัสดุและวิธีการ*: ข้อเข่าจากศพ จำนวน 22 เข่า ที่ไม่เคยได้รับการผ่าตัดเข่ามาก่อน*

ผลการศึกษา*: เอ็นไขว้หน้ามีความยาวเฉลี่ย 33.1 มิลลิเมตร (30.5-38.7 มิลลิเมตร) และมีความกว้างที่จุดกึ่งกลางเส้นเอ็นเฉลี่ย 11.0 มิลลิเมตร (29.4-38.1 มิลลิเมตร) และมีความกว้างที่จุดกึ่งกลางเส้นเอ็นเฉลี่ย 11.0 มิลลิเมตร (9.8-13.0 มิลลิเมตร) ไม่พบความแตกต่างระหว่าง เพศชายกับเพศหญิง (P>0.05) ไม่พบความแตกต่างระหว่างเข่าขวากับเข่าซ้ายในศพเดียวกัน (P>0.05) และไม่พบความแตกต่างเมื่อเปรียบเทียบความยาว ของเอ็นไขว้หน้ากับ เอ็นไขว้หลังในข้อเข่าข้างเดียวกัน (P>0.05) ที่ระดับความเชื่อมั่นร้อยละ 95 ความกว้างที่จุดกึ่งกลางเส้นเอ็นของเอ็นไขว้หลังมีค่ามากกว่าเอ็นไขว้หน้า อย่างมีนัยสำคัญทางสถิติ (P<0.05) เอ็นไขว้หน้ายึดเกาะอยู่บริเวณส่วนหลังของ Medial surface ของ Lateral femoral condyle โดยจุดยึดเกาะบนกระดูกมีรูปร่างเป็นส่วนของวงกลม แกนของจุดยึดเกาะเอียงไปข้างหน้าเล็กน้อย ทำมุมกับแกนตั้งเฉลี่ย 26.3 องศา ความกว้างของจุดยึดเกาะบนกระดูก Femur และ Tibia เฉลี่ยเป็น 16.3 มิลลิเมตร และ 20.0 มิลลิเมตร ตามลำดับ เอ็นไขว้หลังยึดเกาะอยู่บริเวณส่วนหน้าของ Lateral surface ของ Medial femoral condyle โดยจุดยึดเกาะบนกระดูกมีรูปร่างเป็นส่วนของวงกลมมีแกนอยู่ในระนาบพื้น ความกว้างของจุดยึดเกาะบนกระดูก Femur และ Tibia เฉลี่ยเป็น 19.7 มิลลิเมตร และ 13.9 มิลลิเมตร ตามลำดับ*

สรุป*: ผลการศึกษานี้สามารถนำไปประยุกต์ใช้ในการกำหนดจุดฝังเส้นเอ็นบนกระดูกในการผ่าตัดสร้างเส้นเอ็นสำหรับผู้ป่วยที่มีภาวะข้อเข่าหลวม*

Bone Mineral Density Differences in Hip Fractures of the Elderly

Surat Songviroon, MD, MPH

Department of Orthopaedic, Maharat Nakhonratchasima Hospital, Nakhonratchasima, Thailand

Purpose: *To evaluate the differences in bone mineral density (BMD) between the fracture and non-fracture sides in cases of femoral neck and intertrochanteric fractures in elderly.*
Methods: *A cross-sectional study in elderly patients admitted to Maharat Nakhonratchasima Hospital between March 1, 2012 and September 30, 2012. Each had a diagnosis of femoral neck or intertrochanteric fracture. After applying inclusion and exclusion criteria, one hundred patients were included. All answered the fracture risk assessment tool. BMD was measured by Dual energy X-ray absorptiometry prior to surgery. Data was analyzed statistically.*
Results: *Demographic data from the fracture groups, mean age, and body mass index displayed no statistical differences. BMD measurements were higher on the fracture side than on the non-fracture side and statistically different in nearly all areas of the hip. BMD measurements produced statistical differences in some areas when comparison was made between fracture groups, and between genders. The BMD in males was not statistically different between the femoral neck and intertrochanteric fracture groups, and between the fractured and non-fractured sides.*
Conclusion: *Overall the BMD was statistically different between the fracture and non-fracture sides. In addition, the BMD was not statistically different between the femoral neck fracture and intertrochanteric fracture groups in some areas.*

Keywords: *Bone mineral density, femoral neck fracture, intertrochanteric fracture*

The Thai Journal of Orthopaedic Surgery: 37 No.1: 9-14
Full text. e journal: *http://www.rcost.or.th, http://thailand.digitaljournals.org/index.php/JRCOST*

Introduction

Thailand's elderly population has increased, as has the prevalence and incidence of osteoporosis and osteopenia in both genders[1-7]. Osteoporosis is the leading risk factor for fractures, mortality rate[8-12], increased budget expense[13], decreased daily activities, and quality of life[14]. The World Health Organization defines the diagnosis of osteoporosis by bone mineral density (BMD), determined by Dual energy X-ray absorptiometry[15,16], and uses the fracture risk assessment tool (FRAX ®) to evaluate fracture risk[17,18]. There are reports that BMD is higher in femoral neck than in intertrochanteric fractures in all age groups[19-21], but was not statistically significant in age groups (p 0.44), in gender between hip fracture and control groups (non-fracture) (p 0.61), in total BMD (p 0.16), and in the greater and lesser trochanter areas. BMD values between femoral neck fracture and non-fracture groups were (p 0.59) and (p 0.21) respectively. Statistical significance was noted in the BMD of the greater trochanter area compared with the neck of the femur and the neck area, and between femoral neck fracture and non-fracture groups[22].

Correspondence to: Songviroon S, Department of Orthopaedic, Maharat Nakhonratchasima Hospital, Nakhonratchasima, Thailand
E-mail: suratortho@yahoo.com

Gnudi et al. studied BMD in post-menopausal women, and reported that the BMD difference was statistically significant between hip fracture and non-fracture (control) groups, intertrochanteric fracture and controlled non-fracture groups, but not statistically significant between femoral neck fracture and non-fracture groups[23].

The Orthopaedic Department of Maharat Nakhonratchasima Hospital admitted 689 cases of elderly hip fracture in 2011, of whom 421 underwent surgery. There are no previous studies of BMD in Thai hip fracture patients, and few overseas studies. This study will present BMD differences between two groups: femoral neck fracture and intertrochanteric fracture groups, between the fracture and non-fracture sides, and between males and females.

Materials and Methods

The Maharat Nakhonratchasima Hospital Institutional Review Board approved this study. It is cross–sectional, and included 100 patients admitted to the Orthopaedic Department, Maharat Nakhonratchasima Hospital from March 1, 2012 to September 30, 2012. Included were patients diagnosed with intertrochanteric or femoral neck fracture, who accepted admission to the study, who gave informed consent, and whose age was greater than 50 years. Exclusion criteria included previous

implantation in a different hip fracture, pathological fracture from cancer**,** cardiovascular aneurysm or previous stroke, and sero-positive for HIV antibody. All patients and/or close relatives answered the FRAX ® tool questionnaire, and BMD was measured shortly after admission prior to definitive surgical treatment. All patients were examined in the supine position with skin traction, without further manipulation. The hip area BMD alone was measured; the spine and wrist areas were not examined. BMD was measured by a single radiological technologist using a Hologic, Discovery W model (serial #81497). Data was analyzed using mean, standard deviation, chi-square test, and unpaired Student's t-Test. Statistical significance was accorded when $P<0.05$.

Table 1 Demographic data

Data	Femoral neck fracture group	Intertrochanteric fracture group	
Number (Cases)	47	53	
Age Range (years)	55-92	54-89	
Average age ± SD	74.3 ± 8.8	77.0 ± 8.1	*P*-value 0.1165
Left / Right side (Cases)	28 / 19	29 / 24	
Male / Female (Cases)	10 / 37	19 / 34	
Body mass index (BMI) (kg/m^2) Mean ± SD	21.2 ± 6.2	20.5 ± 8.3	*P*-value 0.6602

Results

Table1 shows patient data for both groups, with no statistical significance in average age, or body mass index. Male patients were fewer than female, as previously reported in Thailand[5]. Males suffered fewer fractures than did females, and the left side predominated in both groups. Falls are the most common cause of fracture, also reported previously[24]. Thirty-three cases in the femoral neck fracture group resulted from falls and four were idiopathic. Falls caused all fractures in the intertrochanteric group. Duration of symptoms prior to admission ranged from 1-40 days with an average of 9.48 days (SD ± 6.94) in the femoral neck group, and from 1-12 days with an average of 2.36 days (SD ± 1.98) in the intertrochanteric group. Using the Chi–square test, subgroups were evaluated for BMD versus duration of symptoms. No statistical differences were uncovered.

The FRAX ® tool questionnaire data indicated that each group included three cases of previous wrist fracture from falls. There were two cases of hip fracture in parents in the former group but no cases in the latter group. Glucocorticoid usage was found five cases in the former, and six in the latter group. Also found were current tobacco usage: 9 cases in the former group and 10 cases in the latter group; and alcohol consumption 13 and 9 cases. Rheumatoid arthritis occurred in only one case (interfrochanteric group). There were no cases of previous gynecological surgery, chemotherapy for breast cancer, malabsorption syndrome, chronic liver disorders, organ transplant, diabetes mellitus type 1, or osteogenesis imperfecta in either group. Secondary osteoporosis from premature menopause: 4 cases in the former group and 3 cases in the latter group. Gastrointestinal problems: three cases in each group. Common comorbidity diseases: hypertension 20/24 cases, diabetes mellitus 8/11 cases. Thus the difference between the two groups was minimal.

Table 2 Comparison of BMD by fracture area, and by side (fracture and non-fracture)

	Femoral neck fracture group		Intertrochanteric fracture group		*P*-value			
Area	Fracture side (A)	Non-fracture side (B)	Fracture side (C)	Non-fracture side (D)	(A) vs (B)	(A) vs (C)	(C) vs (D)	(B) vs (D)
Neck	0.5±0.16	0.47±0.14	0.45±0.16	0.45±0.13	0.0167	0.0156	0.5900	0.3794
Troch	0.45±0.12	0.40±0.10	0.47±0.13	0.37±0.10	0.0004	0.3052	0.0000	0.1086
Inter	0.80±0.22	0.70±0.18	0.89±0.25	0.69±0.20	0.0001	0.0636	0.0000	0.7829
Total	0.68±0.17	0.58±0.16	0.73±0.20	0.56±0.15	0.0000	0.2210	0.0000	0.5777
Ward	0.54±0.20	0.31±0.16	0.42±0.21	0.28±0.12	0.0000	0.0071	0.0000	0.3337

Note – Mean±Standard Deviation

In both fracture groups, the average BMD on the fracture side was higher than the non-fracture side with statistically significance at all areas except the neck area of the intertrochanteric fracture group. Comparison between the fracture groups yielded a statistically significant difference in the neck and ward area on the fracture side, but no statistical significance at trochanter, intertrochanter and total area on the fracture side, and all areas on the non-fracture side.

Table 3 Comparison of BMD by fracture area and by side in male

	Femoral neck fracture group		Intertrochanteric fracture group		*P*-value			
Area	Fracture side (A)	Non-fracture side (B)	Fracture side (C)	Non-fracture side (D)	(A) vs (B)	(A) vs (C)	(C) vs (D)	(B) vs (D)
Neck	0.58±0.13	0.56±0.15	0.54±0.17	0.51±0.16	0.6489	0.4720	0.3141	0.3778
Troch	0.58±0.12	0.48±0.12	0.56±0.13	0.44±0.11	0.0561	0.6381	0.0004	0.3062
Inter	1.05±0.20	0.87±0.20	1.09±0.28	0.86±0.19	0.0086	0.7084	0.0003	0.9361
Total	0.87±0.17	0.71±0.21	0.88±0.22	0.69±0.15	0.0562	0.8827	0.0002	0.6796
Ward	0.68±0.20	0.42±0.24	0.52±0.22	0.32±0.14	0.0449	0.0691	0.0019	0.1543

Looking at the male subgroup alone, the BMD of both fracture groups displayed higher values on the fracture side. These were statistically significant different in the intertrochanteric and ward areas of the femoral neck fracture group and in nearly all areas, except in the neck of the intertrochanteric fracture group. There was no statistical significance when comparing the fracture groups in all areas, both on the fracture and the non-fracture sides.

Table 4 Comparison of BMD by fracture area and by side in female

	Femoral neck fracture group		Intertrochanteric fracture group		*P*-value			
Area	Fracture side (A)	Non-fracture side (B)	Fracture side (C)	Non-fracture side (D)	(A) vs (B)	(A) vs (C)	(C) vs (D)	(B) vs (D)
Neck	0.52±0.16	0.43±0.11	0.41±0.13	0.41±0.09	0.0043	0.0024	0.8091	0.3326
Troch	0.41±0.10	0.38±0.09	0.43±0.11	0.33±0.07	0.0015	0.4996	0.0000	0.0097
Inter	0.73±0.17	0.66±0.15	0.77±0.15	0.60±0.13	0.0023	0.2376	0.0000	0.0751
Total	0.63±0.14	0.54±0.12	0.64±0.13	0.49±0.10	0.0000	0.7189	0.0000	0.0571
Ward	0.50±0.18	0.28±0.12	0.37±0.18	0.26±0.11	0.0000	0.0048	0.0008	0.5251

In the female subgroup, the BMD of both fracture groups was higher on the fracture side, a result similar to that found in males (table3). There were statistically significant differences in all areas on the fracture side, neck and ward area on the non-fracture side of the femoral neck fracture group and nearly all areas, except the neck on the fracture side, and the inter area on the non-fracture side of intertrochanteric fracture group.

Table 5 Comparison of BMD by fracture area and by side (both genders)

	P-value			
	Femoral neck fracture group		Intertrochanteric fracture group	
Area	Fracture side (Male vs Female)	Non-fracture side (Male vs Female)	Fracture side (Male vs Female)	Non-fracture (Male vs Female)
Neck	0.2468	0.4072	0.0024	0.0056
Troch	0.0000	0.0030	0.0004	0.0000
Inter	0.0000	0.0007	0.0000	0.0000
Total	0.0000	0.0015	0.0000	0.0000
Ward	0.0104	0.0127	0.0132	0.1180

BMD comparison between genders were statistically significant in nearly all areas. Exceptions were the neck area in femoral neck fracture group on both sides, and the ward area of the intertrochanteric fracture group on the non-fracture side.

Discussion

BMD comparison between fracture groups for both genders, displayed statistically significant differences at the neck and ward of the femoral neck fracture group, with no statistical significant difference in other areas, nor in any area of the intertrochanteric fracture group. Chi-Chuan Woo[22] reported statistically significant differences in the greater trochanter area, but none in the total, lesser trochanter, and neck areas. BMD comparison between fracture groups (separating the genders) yielded no areas of statistical significance within the male subgroup in both the fracture and non-fracture side. However, BMD in the female subgroup did show statistical significance in some areas. Susan L et al. reported that trochanteric BMD was 13% lower in women and 11% lower in men for those patients with trochanteric fractures, compared to those with femoral neck fracture ($P < 0.01$)[25].

Comparison between the fracture and non-fracture sides yielded a mean BMD that was higher in the former group in all areas. Both fracture groups and both genders displayed statistical significance in nearly all of the areas in the overall trend. This is contrary to the study of Jacqueline R et al.[26] which showed that femoral neck bone density was lower in subjects with hip fractures when compared with non-fracture subjects (p-Value 0.0001). Chi-Chuan Woo[22] reported that the BMD of both groups were lower on the fracture side than non-fracture side in total, greater and lesser trochanter, and neck areas.

Comparison between genders confirmed higher mean BMD values in males, and there were statistically significant in nearly all areas, between fracture and non-fracture sides, and between fracture groups. This finding is similar to that of many others [3,7,25]. Jane A. Cauley et al. reported a study in women in which the BMD was found to be lower in a femoral neck fracture group than in an intertrochanteric fracture group. Both results were statistically significant compared to a control (no-fracture group)[26]. Male BMD measurements between femoral neck and intertrochanteric fracture groups were not statistically significant in our study. Because number of male sample in this study was small, results should be used with caution.

There are limitations to this study: few studies available for review, the number of appropriate cases, short period of BMD examination prior to definitive surgical treatment, available radiological support, and the small number of prior studies. An increased number of reports, on larger populations would yield information of greater validity.

Conclusion

Overall, the BMD was statistically significant between the fracture and non-fracture sides and in some areas between the femoral neck and intertrochanteric fracture groups.

Acknowledgements

The author wishes to thank Miss Tanawadee Kluankrathok, B.Sc.(RT), Department of Nuclear Medicine, Maharat Nakhonratchasima Hospital; Dr.Yothi Tongpenyai, MD., Ph.D., Department of Pediatrics, Maharat Nakhonratchasima Hospital; Assoc. Prof. Suppasin Soontrapa B.Sc., MD., Department of Orthopaedics, Faculty of Medicine, KhonKaen University; and Assoc. Prof. Sattaya Rojanasthien MD., Department of Orthopaedic Surgery, Faculty of Medicine, Chiang Mai University, for their help and suggestions in the preparation of this publication.

References

1. Foundation of Thai gerontology research and development. Elderly situation report 2006. Bangkok. October printing co.ltd. 2007.
2. Thailand Population 2008. Institute for population and research. Mahidol university. 2008; 17: 1.
3. Limpaphayom KK, Taechakraichana N, Jaisamrarn U, Bunyavejchevin S, Chaikittisilpa S, Poshyachinda M, et al. Bone mineral density of lumbar spine and proximal femur in normal Thai women. J Med Assoc Thai 2000; 83: 725-31.
4. Limpaphayom KK, Taechakraichana N, Jaisamrarn U, Bunyavejchevin S, Chaikittisilpa S, Poshyachinda M, et al. Prevalence of osteopenia and osteoporosis in Thai women. Menopause 2001; 8: 65-9.
5. Lau EM, Lee JK, Suriwongpaisal P, Saw SM, Das De S, Khir A, et al. The incidence of hip fracture in four Asian countries: the Asian Osteoporosis Study (AOS). Osteoporos Int 2001; 12: 239-43.
6. Shahla A. Validity of bone mineral density and WHO fracture risk assessment thresholds in hip fractures. Arch Iran Med 2011; 14: 352-4.
7. Pongchaiyakul C, Apinyanurag C, Soontrapa S, Soontrapa S, Pongchaiyakul C, Nguyen TV, et al. Prevalence of osteoporosis in Thai men. J Med Assoc Thai 2006; 89: 160-9.
8. Randell A, Sambrook PN, Nguyen TV, Lapsley H, Jones G, Kelly PJ, et al. Direct clinical and welfare costs of osteoporotic fractures in elderly

men and women. Osteoporos Int 1995; 5: 427-32.
9. Ryan PJ. Overview of role of BMD measurements in managing osteoporosis. Semin Nucl Med 1997; 27: 197-209.
10. Marshall D, Johnell O, Wedel H. Meta-analysis of how well measures of bone mineral density predict occurrence of osteoporotic fractures. BMJ 1996; 312: 1254-9.
11. Chariyalertsak S, Suriyawongpaisal P, Thakkinstain A. Mortality after hip fracture in Thailand. Int Orthop 2001; 25: 294-7.
12. Vaseenon T, Luevitoonvechkij S, Wongtriratanachai P, Rojanasthien S. Long-term mortality after osteoporotic hip fracture in Chiang Mai, Thailand. J Clin Densitom 2010; 13: 63-7.
13. Woratanarat P, Wajanavisit W, Lertbusayanukul C, Loahacharoensombat W, Ongphiphatanakul B. Cost analysis of osteoporotic hip fractures. J Med Assoc Thai 2005; 88S5: S96-104.
14. Pongchaiyakul C, Songpattanasilp T, Taechakraichana N. Burden of osteoporosis in Thailand. J Med Assoc Thai 2008; 91: 261-7.
15. Assessment of fracture risk and its application to screening for postmenopausal osteoporosis. Report of a WHO study group. World Health Organ Tech Rep Ser 1994; 843: 1-129.
16. Kanis JA, Melton LJ 3rd, Christiansen C, Johnston CC, Khaltaev N. The diagnosis of osteoporosis. J Bone Miner Res 1994; 9: 1137-41.
17. Kanis JA. Assessment of osteoporosis at the primary health-care level. Technical report. WHO Collaborating Centre, University of Sheffield, UK; 2007.
18. Kanis JA, Johnell O, Oden A, Johansson H, McCloskey E. FRAX TM and the assessment of fracture probability in men and women from the UK. Osteoporosis Int 2008; 19: 385-97.
19. Bartl R, Frisch B. Osteoporosis: Diagnosis, Prevention, Therapy. Berlin, Germany: Springer; 2009.
20. Adams JE. Dual-energy X-ray absorptiometry. In: Grampp S, ed. Radiology of Osteoporosis. Berlin, Germany: Springer 2008; 105–24.
21. Morgan EF, Bayraktar HH, Keaveny TM. Trabecular bone modulusdensity relationships depend on anatomic site. J Biomech 2003; 36: 897-904.
22. Wu CC, Wang CJ, Shyu YI. Variations in bone mineral density of proximal femora of elderly people with hip fractures: a case-control analysis. J Trauma 2011; 71: 1720-5.
23. Gnudi S, Ripamonti C, Lisi L, Fini M, Giardino R, Giavaresi G. Proximal femur geometry to detect and distinguish femoral neck fractures from trochanteric fractures in postmenopausal women. Osteoporos Int 2002; 13: 69-73.
24. Melton LJ 3rd. Epidemiology of fractures. In: Riggs BL, Melton LJ 3rd, editors. Osteoporosis: etiology, diagnosis, and management. 2nd ed. Philadelphia-New York: Lippincott-Raven; 1995. p. 225-47.
25. Greenspan SL, Myers ER, Maitland LA, Kido TH, Krasnow MB, Hayes WC. Trochanteric bone mineral density is associated with type of hip fracture in the elderly. J Bone Miner Res 1994; 9: 1889-94.
26. Center JR, Nguyen TV, Pocock NA, Eisman JA. Volumetric bone density at the femoral neck as a common measure of hip fracture risk for men and women. J Clin Endocrinol Metab 2004; 89: 2776-82.
27. Cauley JA, Lui LY, Genant HK, Salamone L, Browner W, Fink HA, et al. Risk Factors for Severity and Type of the Hip Fracture. J Bone Miner Res 2009. 24: 943-55.

ความแตกต่างของค่าความหนาแน่นของมวลกระดูกในผู้ป่วยสูงอายุที่มีกระดูกสะโพกหักที่ส่วนคอและระหว่างโทรแคนเตอร์

สุรัตน์ ส่งวิรุฬห์, พบ, สม (บริหารสาธารณสุข)

วัตถุประสงค์: *เพื่อศึกษาความความแตกต่างของค่าความหนาแน่นของมวลกระดูกบริเวณสะโพกระหว่างข้างที่หักและไม่หักในผู้ป่วยสูงอายุที่มีกระดูกสะโพกหัก*

วัสดุและวิธีการ: *เป็นการศึกษาแบบการสำรวจ โดยวิธีเลือกผู้ถูกสำรวจเพื่อให้ได้สถิติคล้ายคลึงกับการสำรวจพลเมืองทั้งหมด ในผู้ป่วยสูงอายุที่มานอนรักษาตัวที่โรงพยาบาลมหาราชนครราชสีมา ระหว่างวันที่ 1 มีนาคม พ.ศ.2555 ถึงวันที่ 30 กันยายน พ.ศ.2555 ซึ่งได้รับการวินิจฉัยว่ามีกระดูกสะโพกหักที่ส่วนคอและระหว่างโทรแคนเตอร์ จำนวน 100 รายซึ่งกำหนดเกณฑ์เข้าร่วมและคัดออกไว้ ผู้ที่เข้าร่วมการศึกษาทุกรายได้ตอบแบบสอบถามตามเครื่องมือประเมินความเสี่ยงกระดูกหักและรับการตรวจค่าความหนาแน่นของมวลกระดูกบริเวณสะโพกด้วยเครื่องตรวจวัดมวลกระดูกก่อนรับการรักษาด้วยการผ่าตัด นำข้อมูลที่ได้มาวิเคราะห์ทางสถิติ*

ผลการศึกษา: *ลักษณะข้อมูลพื้นฐานระหว่างบริเวณกระดูกที่หัก อายุเฉลี่ย ดัชนีมวลกาย ไม่มีความแตกต่างอย่างมีนัยสำคัญทางสถิติ ค่าความหนาแน่นของมวลกระดูกบริเวณสะโพกข้างที่หักมีค่าเฉลี่ยสูงกว่าข้างที่ไม่หัก โดยมีความแตกต่างอย่างมีนัยสำคัญทางสถิติเกือบทุกตำแหน่ง และมีความแตกต่างอย่างมีนัยสำคัญทางสถิติในบางตำแหน่งเมื่อเปรียบเทียบระหว่างกลุ่ม ตำแหน่งที่หัก และเพศ ในเพศชายไม่มีความแตกต่างอย่างมีนัยสำคัญทางสถิติค่าความหนาแน่นของมวลกระดูกทุกตำแหน่งเมื่อเปรียบเทียบระหว่างกลุ่มของข้างที่หักและข้างที่ไม่หัก*

สรุป: *ค่าความหนาแน่นของมวลกระดูกมีความแตกต่างอย่างมีนัยสำคัญทางสถิติระหว่างข้างที่หักและไม่หักในภาพรวม*

The Thai Journal *Of* Orthopaedic Surgery

The Official Journal of the Royal College of Orthopaedic Surgeons of Thailand

ISSN 0125-7552

Volume 37 / Number 2-4 April-October 2013

The Council Members of the Royal College of Orthopaedic Surgeons of Thailand (RCOST) 2012-2014

President	**Thavat Prasartritha, MD**
Immediate Past President	**Adisorn Patradul, MD**
President Elect	**Sukit Saengnipanthkul, MD**
1st Vice-President	**Banchong Mahaisavariya, MD**
2nd Vice-President	**Aree Tanavalee, MD**
Registrar	**Chumroonkiet Leelasestaporn, MD**
Treasurer	**Thawee Songpatanasilp, MD**
Secretary General	**Keerati Chareancholvanich, MD**
Assistant Secretary General	**Charlee Sumettavanich, MD**
Promotion	**Thana Turajane, MD**
Council Members	**Sumroeng Neti, MD**
	Pijaya Nagavajara, MD.
	Kanyika Chanmiprasas, MD
	Preecha Chalidapong, MD
	Warat Tassanawipas, MD
	Chiroj Sooraphanth, MD
	Thipachart Bunyaratabandhu, MD
Advisory Board	**Samak Bukkanasen, MD**
	Natee Rukpollamuang, MD
	Direk Israngkul, MD
	Suprija Mokkhavesa, MD
	Charoen Chotigavanich, MD
	Vinai Parkpian, MD
	Pongsak Vathana, MD
	Prasit Gonggetyai, MD
	Chaithavat Ngarmukos, MD
	Thamrongrat Keokarn, MD
	Suthorn Bavonratanavech, MD
	Wichien Laohacharoensombat, MD
	Saranatra Waikakul, MD

the 35th Annual Meeting of RCOST 2013
Pattaya, Chonburi Province, Thailand on October 20-22, 2013

ราชวิทยาลัยแพทย์ออร์โธปิดิกส์แห่งประเทศไทย

The Royal College of Orthopaedic Surgeons of Thailand

ขอเรียนเชิญแพทย์และผู้สนใจเข้าร่วมฟังการบรรยาย

วันอาทิตย์ที่ 20 ตุลาคม 2556 เวลา 11.30-13.00 น.

Interactive workshop:

งานวิจัยสำหรับการขอกำหนดตำแหน่งนายแพทย์เชี่ยวชาญ

11.30 - 11.40 ปัญหาหนักใจใน ซี 9

11.40 - 12.00 ช่วยอย่างไร...ทำไมไม่ได้
กรรมการ Research Section

12.00 - 12.40 เสวนา...ปริศนาคาใจ
กรรมการผู้ประเมินและผู้เข้าร่วมประชุม

12.40 - 13.00 ราชวิทยาลัยจะทำอย่างไรดี
กรรมการราชวิทยาลัย

The Thai Journal of Orthopaedic Surgery

Current Editorial Board (2013-2014)

Editorial office address: The Royal College of Orthopaedic Surgeons of Thailand
4 th Floor, Royal Golden Jubilee Building, 2 Soi Soonvijai, New Petchburi Road, Bangkapi, Huay Khwang, Bangkok 10310
E-mail: secretariat@rcost.or.th, supawineep@rcost.or.th
Telephone: +66 2 7165436-7
The Journal is free online at http://www.rcost.or.th, http://thailand.digitaljournals.org/index.php/JRCOST

the 35th Annual Meeting of RCOST 2013
Pattaya, Chonburi Province, Thailand on October 20-22, 2013

ราชวิทยาลัยแพทย์ออร์โธปิดิกส์แห่งประเทศไทย

The Royal College of Orthopaedic Surgeons of Thailand

ขอเรียนเชิญแพทย์และผู้สนใจเข้าร่วมฟังการบรรยาย

วันจันทร์ที่ 21 ตุลาคม 2556

RCOST Symposia 1: Ethics & law in orthopaedic practice

- แนวโน้มปัญหาจริยธรรมในวิชาชีพออร์โธปิดิกส์ ศ.นพ. สุกิจ แสงนิพันธ์กูล
- กรณีศึกษาทางจริยธรรมและมาตรฐานวิชาชีพ นพ. ต่อพล วัฒนา
- การเตรียมตัว เมื่อเกิดปัญหาที่อาจถูกฟ้องร้อง นพ. วันชัย ศิริเสรีวรรณ

RCOST Symposia 2: Meet the Jedi Episode II

- นพ. พงษ์ศักดิ์ วัฒนา
- นพ. สุปรีชา โมกขะเวส
- นพ. ก่อกู้ เชียงทอง

RCOST Symposia 3: Tips & pitfalls in researches & publications

(สำหรับการขอตำแหน่งนายแพทย์เชี่ยวชาญ)

Moderator : นพ. วิวัฒน์ สุรางค์ศรีรัฐ

Panelists:

- ศ.เกียรติคุณ นพ. เจริญ โชติกวณิชย์
- รศ.นพ. วินัย พากเพียร
- นพ. ยิ่งยง สุขเสถียร
- นพ. พลวรรธน์ วิทูรกลชิต

RCOST Symposia 4: การเบิกจ่ายวัสดุอุปกรณ์ทางการแพทย์ของ 2 กองทุน

Moderator : นพ.ชาลี สุเมธวาณิชย์

- นพ. การุณย์ คุณติรานนท์ (สปสช)
- คุณ อภิสมา ชาญสืบกุล (กรมบัญชีกลาง)

The Thai Journal of Orthopaedic Surgery Volume 37 Number 2-4 April-October 2013

Contents

สารบัญ

Editorial

"The Thai Orthopaedic Society…… The Learned Society"

Pongsak Yuktanandana, MD

Department of Orthopaedics, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand

First of all, I would like to thank the president of the Royal College of Orthopaedic Surgeons of Thailand, Dr. Thavat Prasartritha and the Council Members for the appointment to be editor of "The Thai Journal of Orthopaedic Surgery". I also would like to thank Professor Aree Tanavalee and Professor Sittisak Honsawek for helping to form the editorial board. I am very grateful to all editorial board members who would like to contribute their knowledge and experience to form our learned "Thai Orthopaedic Society".

The year 2014 will mark the 50th anniversary of three university hospitals who's Departments of Orthopaedics separated from their Department of Surgery including: Department of Orthopaedic Surgery, Siriraj Hospital, Department of Orthopaedics, King Chulalongkorn Memorial Hospital, and Department of Orthopaedics, Chiangmai University Hospital. Orthopaedic residency training started a few years before that separation. The learning society started in 1966 in Bangkok Metropolitan Administration General Hospital, where a group of orthopaedic surgeons got together and formed Thai Orthopaedic Club which developed to become the Royal College of Orthopaedic Surgeons of Thailand. We have had inter-hospital grand rounds, lectures and workshops to help each other to improve our knowledge and experience to serve people in the country for nearly fifty years.

The ASEAN region is one of the fastest growing regions in the world. By the year 2015, the ASEAN Economic community shall be integrated to be a single market and production base, a highly competitive economic region and equitable economic development. This economic integration will affect not only exchange trading and labor work but also medical services across the region. Every country in ASEAN declared the readiness to be a medical hub of the region. Thailand has the largest number of orthopaedic surgeons in the ASEAN. Membership of the Royal College of Orthopaedic Surgeons of Thailand is approaching 2,000 members while other countries have only a few hundred members. In the beginning era of orthopaedic practice in Thailand, orthopaedic surgeons had to deal with everything from fracture management, spinal problems, adult reconstruction, pediatric orthopaedics, hand and reconstructive surgery as well as musculoskeletal tumors. Orthopaedic surgeons worked mainly in large public hospital.

Now, orthopaedic surgeons in Thailand work in various institutions including: academic institutions, large and small public hospitals and also large numbers work in the private sector. Many orthopaedists were certified by the Royal College and continued their fellowship in subspecialty abroad. As the future of medicine tends towards becoming more specialized, the Thai orthopaedic society also has the largest number of subspecialties. Many subspecialty societies are very active exchanging their knowledge, sharing their experience and training a younger generation to become competent and proficient surgeons. It may be time that we have to reconsider about raising training standards, improving research publications and forming a subspecialty society. We are well prepared and ready to be a leader of orthopaedic practice in the ASEAN region. Let's do it together. Let's learn together.

Does a Saline Load Test Combined with Direct Compression to the Knee Increase Sensitivity in the Assessment of a Traumatic Open Knee Injury?

Surasit Phonglaohaphan, MD, Chonlathan Iamsumang, MD

Department of Orthopaedic Surgery, Lampang Hospital, Lampang, Thailand

Purpose: *To determine whether a saline load test combined with direct compression to the knee increases sensitivity for the assessment of traumatic arthrotomy of the knee.*
Methods: *A total of 40 patients scheduled for elective inpatient knee arthroscopy and total knee arthroplasty (TKA) were prospectively enrolled. A 7 to 8 ml stab wound for arthrotomy was performed at the inferolateral site of the knee for cases who would receive arthroscopy and at the inferomedial site for the TKA cases. Then, 50 ml of normal saline was injected into the knee joint while observing fluid leakage from the arthrotomy site. It was considered a positive saline load test if there was any leakage. If not, subsequent direct compression was applied to the knee. Any leakage incurred was considered a positive compression test.*
Results: *The saline load test was positive in 13 out of 40 patients and additional 18 patients showed a positive compression test. The sensitivity of the saline load test was 32.5% while that of the compression test was 77.5%.*
Conclusion: *Additional direct compression to the knee increased the sensitivity of saline load tests in the assessment of a small traumatic knee arthrotomy (open knee injury).*

Keywords: *Saline load test, traumatic knee arthrotomy, open knee injury, direct compression*

The Thai Journal of Orthopaedic Surgery: 37 No.2-4: 17-21
Full text. e journal: *http://www.rcost.or.th, http://thailand.digitaljournals.org/index.php/JRCOST*

Introduction

Traumatic arthrotomy of the knee can be clinically diagnosed by the mechanism of injury, type of wound and physical examination. Combined clinical, radiographic and saline load tests also help achieve the diagnosis. Delayed or missed diagnosis may result in severe complications such as septic arthritis or septicemia. The saline load test is a simple method and is easily diagnosed by evidence of saline leakage from the wound. However, in cases of small wounds, the diagnosis is frequently difficult. Many articles have been published about the accuracy and sensitivity of saline load tests to diagnose traumatic arthrotomy of the knee[1-6]. Most of them indicated that the saline load test has a low detection rate[3-6]. However, this method has been routinely used in clinical practice despite insufficient literature discussing its effectiveness. In this study, direct compression to the knee joint after a saline injection was performed and hypothesized that the use of a combined method may increase sensitivity of the diagnosis. To our knowledge, there are no studies that describe the saline load test combined with direct compression.

Correspondence to: Phonglaohaphan S, Department of Orthopaedic Surgery, Lampang Hospital, Lampang 52000, Thailand
E-mail: surasitmd@gmail.com

Patients and methods

Our study was designed as a prospective analytical study conducted by two orthopaedists at Lampang Hospital, from November 2012 to April 2013. Forty patients scheduled for elective inpatient knee arthroscopy and total knee arthroplasty (TKA) were enrolled, comprising of 22 males and 18 females. The patients' data of sex, age, height and weight were obtained from medical records and their body mass index (BMI) calculated. Exclusion criteria were history of traumatic knee injury, clinical manifestation of septic arthritis and revision knee surgery. This research was approved by the Ethics Committee of Lampang Hospital prior to data collection. Informed consent was given by all patients who participated in this study.

After preparation for the knee operation, a stab wound arthrotomy was performed at the inferolateral parapatellar site for arthroscopy and inferomedial site for TKA, with a No.11 blade at 30-degrees of knee flexion. The length of the incision was approximately 7-8 mm (Fig. 1) that of which is required for operative procedure. A blunt probe was inserted and the knee was extended, the probe was advanced into the suprapatellar pouch to ensure intraarticular placement (Fig. 2). After removal of the blunt probe, the knee was placed in full extension. Fifty ml of saline was then injected intraarticularly via an 18-gauge needle, at the superolateral or superomedial site, at a rate of

approximately 5 ml per second (Fig. 3). The surgeon and assistant observed for fluid leakage from the arthrotomy site. If there is saline leakage, the result was considered a positive saline load test. In contrast, if there was no leakage, the result was considered negative. In the latter group, further direct compression over the upper portion of patella was applied by the surgeon (Fig. 4). The compression force was approximated at 5-7 kg controlled by practicing the compression on the baby weighing scale (Fig. 5). If there was any leakage, the result was considered a positive compression test, and considered a negative compression test if there was no leakage. After completing the test, the planned operative procedure was performed.

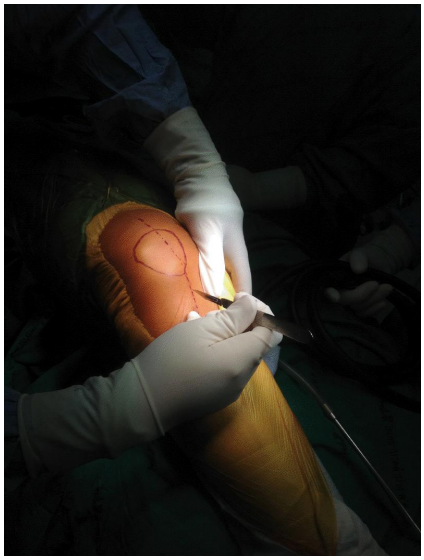


Fig. 1 A standard stab wound arthrotomy at the inferomedial site of the knee

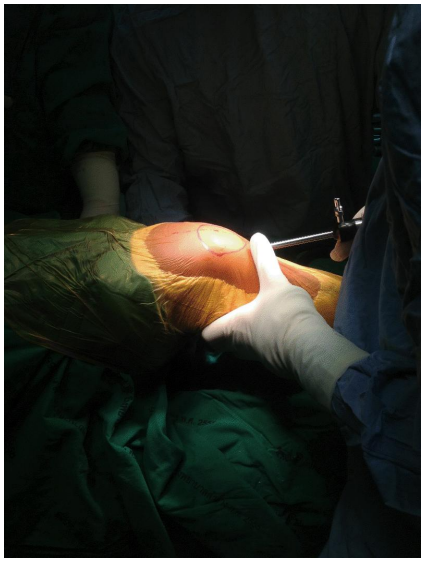


Fig. 2 Intraarticular placement is confirmed with a blunt probe

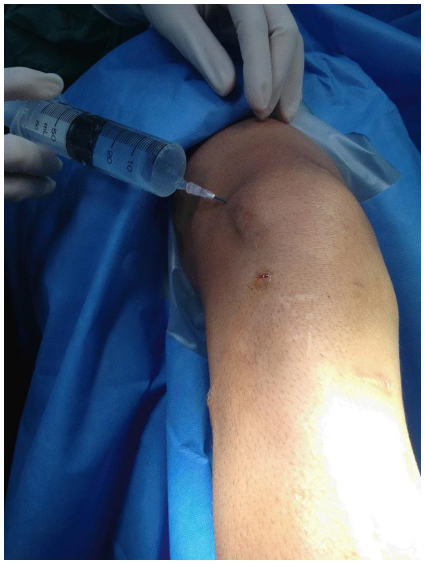


Fig. 3 A saline load test was performed and observation of saline leakage from the arthrotomy

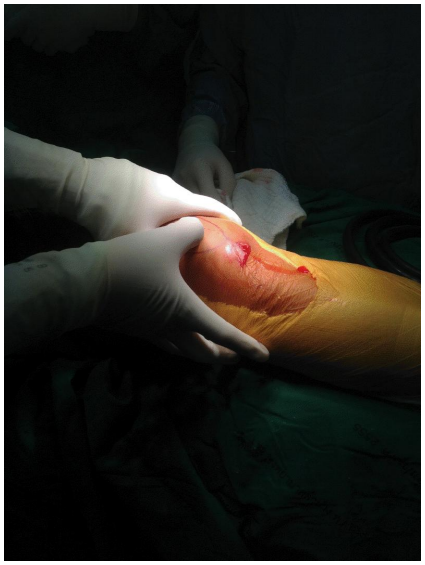


Fig. 4 Compression test on the knee and saline leakage from the arthrotomy wound

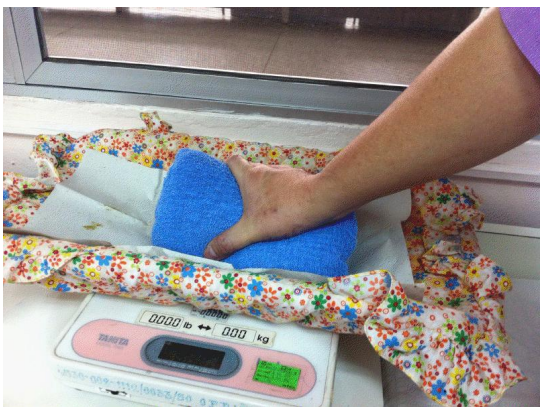


Fig. 5 Test of compression force on electronic baby weighing scale

Table 1 Patient demographic data

	Male	Female	Total
No. of subjects	22	18	40
Age (years)	47.5 (20-74)	61 (32-79)	53.6 (20-79)
BMI (kg/m^2)	23.7 (18.0-31.0)	23.5 (17.9-30.4)	23.6 (17.9-31.0)

Table 2 Saline load test and additional compression test

	Total No. of case	No. of positive test	Sensitivity	95% Confidence Interval
Saline load test	40	13	32.5%	18.6%-49.1%
Saline load test with additional compression test	40	31	77.5%	61.5%-89.2%

Results

There were 40 participants: 22 male and 18 female patients. The average age was 53.6 years (range 20-79 years) and the average BMI was 23.6 (range 17.9-31.0) as shown in table 1.

In this study, 13 of the 40 patients had a positive saline load test alone without compression on the knee. Eighteen additional patients had a positive test with subsequent direct compression to the knee. Thus, the sensitivity of the saline load test alone was 32.5% (95% confidence interval 18.6%-49.1%) and with the additional compression was 77.5% (95% confidence interval 61.5%-89.2%), as demonstrated in table 2. The false-negative rate of saline load tests and additional compression tests were 67.5% and 22.5%, respectively.

Discussion

Large traumatic arthrotomy of the knee can be diagnosed clinically, but small arthrotomies may require a saline load test for diagnosis in routine clinical practice, despite little documented effectiveness of this test[3-6]. In this study, we performed small artificial arthrotomies in elective patients that received arthroscopy and TKA surgery. We found that the saline load test of 50 ml had poor sensitivity in the diagnosis of known small knee arthrotomies. The sensitivity was found to be only 32.5% and lower than the previous studies that have found the sensitivity to be between 36% and 46%[3-6], using 50 to 60 ml of normal saline.

This study used a fixed saline volume of 50 ml. Nevertheless, previous studies have used higher volumes of saline to determine if the sensitivity of saline load tests improved. Keese et al.[3] found that, in order to increase the sensitivity to 95%, 194 ml of saline had to be used. Nord et al.[5] discovered that, as much as 175 ml of normal saline had to be used to increase the sensitivity to 99%. However, this amount of normal saline cannot be used in clinical practice because of the pain from massive joint stretching.

Tornetta et al.[4] performed dynamic tests by subsequent passive range of motion of the knee 0 to more than 90 degrees and also found low sensitivity of only 43%.

Metzger et al.[6] in 2012, compared normal saline (NS) and methylene blue (MB) injections and found that the sensitivity of saline load tests were 31% in the MB group and 34% in the NS group. They concluded that the saline load test, with or without the addition of MB dye, may not be an appropriate diagnostic test for traumatic knee arthrotomies.

In our study, additional subsequent compression upon the knee joint was performed in the group of negative saline load tests. We found an improvement of sensitivity of up to 77.5%. This could be from the increase of capsular distention by the pressure effect, resulting in extravasation of fluid from the incision wound. However, the limitation of this study was that the accuracy of the additional compression force may vary. Although the surgeons practiced pressing on baby weighing scales several times before starting the research for the required weight of approximately 5-7 kg, the force of compression in routine clinical practice will vary depending on the individual physician, size of the knee and tolerance of pain in each patient.

Conclusion

Our study suggested that subsequent direct compression to the injured knee increased sensitivity of saline load tests in the diagnosis of traumatic knee arthrotomies. However, a negative

test may not be able to exclude traumatic knee arthrotomies. We thought that increase of capsular distention by pressure effect is the key success factor, resulting in extravasation of fluid from the incision wound.

Acknowledgements

The authors wish to thank Dr.Theerachai Apivathakakul, Department of Orthopaedic Surgery, Chiangmai University, who provided appropriate guidance and comments to this study.

References

1. Patzakis MJ, Dorr LD, Ivler D, Moore TM, Harvey JP Jr. The early management of open joint injuries: a prospective study of one hundred and forty patients. J Bone Joint Surg Am 1975; 57: 1065-70.
2. Voit GA, Irvine G, Beals RK. Saline load test for penertration of periarticular lacerations. J Bone Joint Surg Br 1996; 78: 732-3.
3. Keese GR, Boody AR, Wongworawat MD, Jobe CM. The accuracy of the saline load test in the diagnosis of traumatic knee arthrotomies J Orthop Trauma 2007; 21: 442-3.
4. Tornetta P 3rd, Boes MT, Schepsis AA, Foster TE, Bhandari M, Garcia E. How effective is a saline arthrogram for wounds around the knee?. Clin Orthop Relat Res 2008; 466: 432-5.
5. Nord RM, Quach T, Walsh M, Pereira D, Tejwani NC. Detection of traumatic arthrotomy of the knee using the saline solution load test. J Bone Joint Surg Am 2009; 91: 66-70.
6. Metzger P, Carney J, Kuhn K, Booher K, Mazurek M. Sensitivity of the saline load test with and without methylene blue dye in the diagnosis of artificial traumatic knee arthrotomies. J Orthop Trauma 2012; 26: 347-9.

การฉีดน้ำเกลือเข้าช่องข้อร่วมกับการกดบริเวณข้อเข่าช่วยเพิ่มความไวในการวินิจฉัยภาวะแผลทะลุเข้าช่องข้อเข่าหรือไม่

สุรสิทธิ์ พงษ์เลาหพันธุ์, พบ, ชลทาน เอี่ยมสำอางค์, พบ

วัตถุประสงค์*: เพื่อศึกษาการฉีดน้ำเกลือเข้าช่องข้อเข่า ร่วมกับการกดเพื่อเพิ่มแรงดันบริเวณข้อเข่า สามารถช่วยเพิ่มความไวในการตรวจวินิจฉัยภาวะแผลทะลุเข้าช่องข้อเข่าหรือไม่*

วิธีการศึกษา*: ทำการศึกษาในผู้ป่วยในจำนวน 40 ราย ซึ่งนัดมารักษาโดยการผ่าตัดบริเวณข้อเข่า ได้แก่ การผ่าตัดเปลี่ยนข้อเทียม และการผ่าตัดโดยการส่องกล้องข้อเข่า ทำการศึกษาเมื่อเตรียมผู้ป่วยพร้อมสำหรับทำการผ่าตัดแล้ว ศัลยแพทย์ทำการเจาะข้อเข่าบริเวณที่จะใช้เป็นแผลในการผ่าตัดตามมาตรฐานต่อไป คือบริเวณ inferomedial หรือ inferolateral ของข้อเข่า โดยใช้ใบมีดเบอร์ 11 เจาะจนทะลุเข้าช่องข้อ จากนั้นใช้ blunt probe ตรวจยืนยันว่าแผลนั้นทะลุเข้าช่องข้อจริง จากนั้นศัลยแพทย์ทำการฉีดน้ำเกลือปริมาณ 50 มิลลิลิตรเข้าภายในช่องข้อเข่า แล้วสังเกตว่ามีน้ำเกลือไหลออกมาจากแผลที่เจาะเข้าข้อเข่าหรือไม่ ถ้ามีถือว่าเป็นผลบวก ถ้าไม่มีน้ำเกลือไหลจากแผล ศัลยแพทย์จะใช้มือกดบนข้อเข่าแล้วสังเกตต่อว่ามีน้ำเกลือไหลออกจากแผลหรือไม่ ถ้ามีน้ำเกลือไหลจากแผลถือว่าเป็นผลบวก จากนั้นศัลยแพทย์เริ่มทำการผ่าตัดตามแผนการรักษาของผู้ป่วยแต่ละรายต่อไป*

ผลการศึกษา*: ผู้ป่วยที่เข้าร่วมการศึกษาทั้งหมด 40 ราย ภายหลังการฉีดน้ำเกลือเข้าข้อ พบว่ามีน้ำเกลือไหลออกจากแผล 13 ราย ในกลุ่มที่ไม่มีน้ำเกลือไหลจากแผลแล้วทำการกดบริเวณข้อเข่าต่อ พบว่ามีผู้ป่วยที่มีน้ำเกลือไหลออกจากแผลเพิ่มขึ้นอีก 18 ราย ความไวในการตรวจวินิจฉัยจากวิธีฉีดน้ำเกลือเข้าข้อเข่าเพียงอย่างเดียวคิดเป็นร้อยละ 32.5 แต่เมื่อทำการกดข้อเข่าร่วมด้วย สามารถเพิ่มความไวในการตรวจเป็นร้อยละ 77.5*

สรุป*: การกดบริเวณข้อเข่าร่วมกับการฉีดน้ำเกลือเข้าช่องข้อสามารถเพิ่มความไวในการตรวจวินิจฉัยภาวะแผลทะลุเข้าช่องข้อเข่า*

Reliability of the VDO Clip-based Goniometry Method for Measuring Range of Motion of the Elbow

Pinkawas Kongmalai, MD, Arunwong Thepchatree, MD, Cholawish Chanlalit, MD

MSMC Hospital, Department of Orthopedics, Faculty of Medicine, Srinakarinwirot University, Nakonnayok, Thailand

Purpose: *Telemedicine is an adaptation of internet-based communication for remote patients. The video (VDO) clip-based goniometry method is a type of telemedicine that would be useful for patients who need periodic assessment. A previous report showed the validation of this technique but it did not verify the generalizability or reproducibility of the technique. The purpose of this study was to determine the generalizability and reproducibility of the VDO clip-based goniometry method for measuring the range of motion of the elbow.*

Methods: *Both elbow flexion and extension, and forearm pronation and supination were measured by the specialist in elbow surgery using standard goniometer. On the same day, VDO records of 30 subjects were performed. One week later, the VDO clips were displayed and their range of motion (ROM) was measured using free download software (PicPick, 3.1.0) by an orthopaedic resident (to determine inter-rater/intra-method reliability). One month later, measurements were taken again by the same specialist (to determine intra-rater/intra-method reliability).*

Results: *The intraclass correlation coefficient and the Bland-Altman analysis showed the capability of VDO-clip based goniometry and clinical goniometry by the specialist in elbow surgery and orthopaedic resident especially in elbow extension and forearm supination. For elbow flexion and forearm pronation, the data showed that there was some degree of correlation but not as strong as flexion and extension. The results were reproducible by the specialist in elbow surgery even when the measurements were taken again 1 month later.*

Conclusion: *The VDO clip-based goniometry method for measuring the range of motion of the elbow was reproducible by a specialist in elbow surgery. It was also shown to be possible even if the measurement was obtained by an orthopaedic resident. This offers a great opportunity to follow the outcome assessment of patients for whom transportation to a tertiary care center is a significant barrier.*

Keywords: *Elbow range of motion, measurement, telemedicine, VDO clip-based goniometry*

The Thai Journal of Orthopaedic Surgery: 37 No.2-4: 23-28
Full text. e journal: *http://www.rcost.or.th, http://thailand.digitaljournals.org/index.php/JRCOST*

Introduction

With advancements in internet-based communication, adaption to the technology for the use in clinical assessments of patients is proving interesting. Telemedicine, a service delivered at a distance using this technology, has been experiencing rapid growth with new clinical applications and new products appearing frequently. These services include evaluation and treatment, as well as education, consultation, and coordination of care. They have shown beneficial results in neurology, psychiatry, and rehabilitation [1-4]. To date, few studies have investigated standard assessment tests applied to telemedicine in orthopaedics. Blonna et al. used photography-based goniometry to show the accuracy and reliability of elbow flexion and extension[5]. If one photograph was reliable to indicate the range of motion of the elbow, the video (VDO) clip with the subject in motion should be more reliable because the observer can choose the proper angle to measure from any point of movement.

Reliability in the new measurement technique could include the parameters of validation, generalizability and reproducibility. Chanlalit and Kongmalai have shown that the VDO-clip based goniometry method is technically feasible for measuring the range of motion of the elbow, especially for flexion and extension[6]. But they did not show the inter-rater, intra-method and intra-rater, intra-methods' reliability. This study was designed to investigate the inter-rater, intra-method and intra-rater, intra-methods' reliability to show the generalizability and reproducibility of the VDO-clip based goniometry method.

Correspondence to: Chanlalit C, Department of Orthopaedics, Faculty of Medicine, Srinakarinwirot University, Ongkarak, Nakonnayok 26120, Thailand.
E-mail: chanlalit@hotmail.com

Materials and Methods

Subjects

Sample size calculations (by PASS 2008) indicated that 30 subjects were necessary to detect greater than moderate reliability (alpha = 0.05 and beta = 0.1)[7]. Fifteen women and fifteen men were recruited from the hospital's staff.

An exclusion criterion was that subjects with an obvious deformity of the elbow that precluded the use of standard goniometer.

Methods

The ranges of motion of the elbow from VDO-clips, including flexion, extension, forearm pronation and supination, were measured by free download software (PicPick, 3.1.0, NTe works) by the same landmarks as Chanlalit[6] (Fig. 1). For part 1, we compared the results from a specialist in elbow surgery and an orthopaedic resident to evaluate the generalizability (inter-rater/intra-method reliability).

For part 2, measurements were taken again by the specialist in elbow surgery one month later. This result was compared with the earlier result by the same rater to evaluate the reproducibility (intra-rater/intra-method reliability).

Statistical analysis

The data were analyzed using Bland-Altman analysis that defines the "limits of agreement". This system is based on the mean and standard deviation of the difference between ratings of the same subject[8-10]. The dash line represents the upper limit of agreement for each motion (|average| + 1.96*SD). For discussion later, an upper limit of agreement at 10 degrees is used to accept or refuse the VDO clip-based technique because if we used the upper limit of agreement at 15 degrees, the percentage of measurement within this limit would be very high. In clinical practice, 5 degrees difference might not be significant.

The intra-class correlation coefficient (ICC) two-way mixed model on absolute agreement was used to analyze measurement reliability[11]. The values of the ICC can range from 0 to 1, with a higher value indicating better reliability. An ICC of less than 0.40 was considered as poor; 0.40 to 0.59 as fair; 0.60 to 0.74 as good, and 0.75 to 1.00 as excellent. In addition, the lower and upper limit of 95% confidence interval of ICC was calculated to provide an estimate of the magnitude of the measurement error. Statistical analysis was performed using the statistical package for social sciences (SPSS) software, version 17.0 for Window.

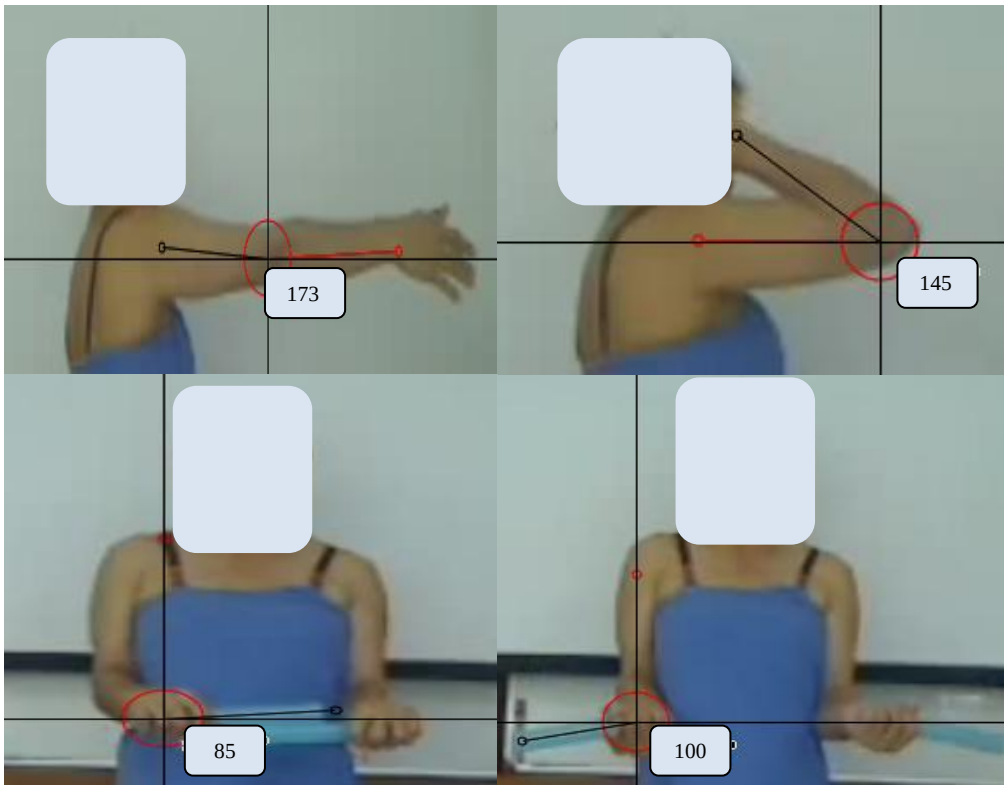
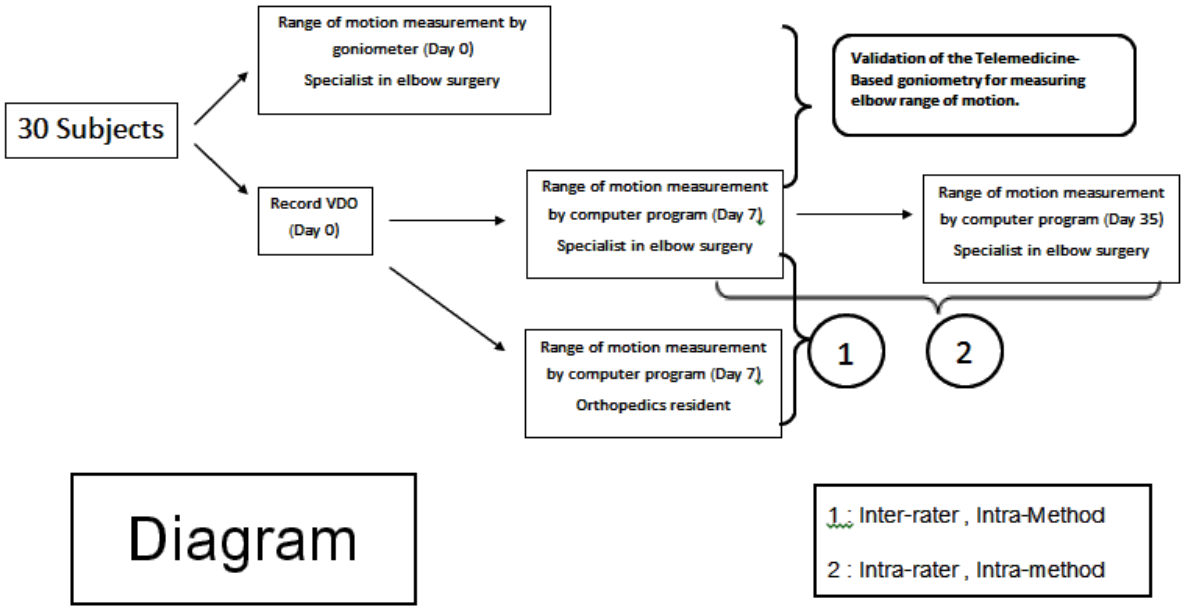


Fig. 1 Range of motion of elbow measurement by computer program



Diagram

Results

Sixty elbows in 30 subjects were included in the study. The average age of subjects was 42 years old. The average weight, height and body mass index of subjects were illustrated in table 1.

Table 1 Demographics data

Variables	Average		
	Male	Female	Overall
Age (years)	41	43	42
Weight (kg)	73	57	65
Height (cm)	176	152	164
BMI (kg/m^2)	23.6	24.7	24.2

Table 2 The ICC between measurements obtained by VDO-based goniometry from the specialist elbow surgeon and orthopaedic resident

Motion	ICC	95% Confidence interval	
		Lower limit	Upper limit
Flexion	0.517	0.304	0.680
Extension	0.719	0.570	0.822
Pronation	0.535	0.326	0.693
Supination	0.659	0.488	0.781

The ICC between measurements obtained by VDO clip-based goniometry from the specialist in elbow surgery and an orthopaedic resident showed elbow extension and forearm supination as good, fair in elbow flexion and forearm pronation (Table 2). The percentage of range of motions within the upper limit of agreement at 10° were 83% for elbow flexion, 95% for elbow extension and 68-78 % for forearm rotation (Fig. 2 and Table 4).

The ICC between measurements obtained by VDO clip-based goniometry from the specialist in elbow surgery in a separate session showed excellent in elbow extension and forearm supination and good in elbow flexion and forearm pronation (Table 3). The percentage of range of motions within the upper limit of agreement at 10 degrees was 95% for elbow flexion, 100% for elbow extension and 82-93% in forearm rotation (Fig. 3 and Table 4).

Table 3 The ICC between measurements obtained by VDO-based goniometry from a specialist elbow surgeon in a separate session

Motion	ICC	95% Confidence interval	
		Lower limit	Upper limit
Flexion	0.638	0.4604	0.767
Extension	0.879	0.806	0.926
Pronation	0.645	0.469	0.772
Supination	0.762	0.631	0.851

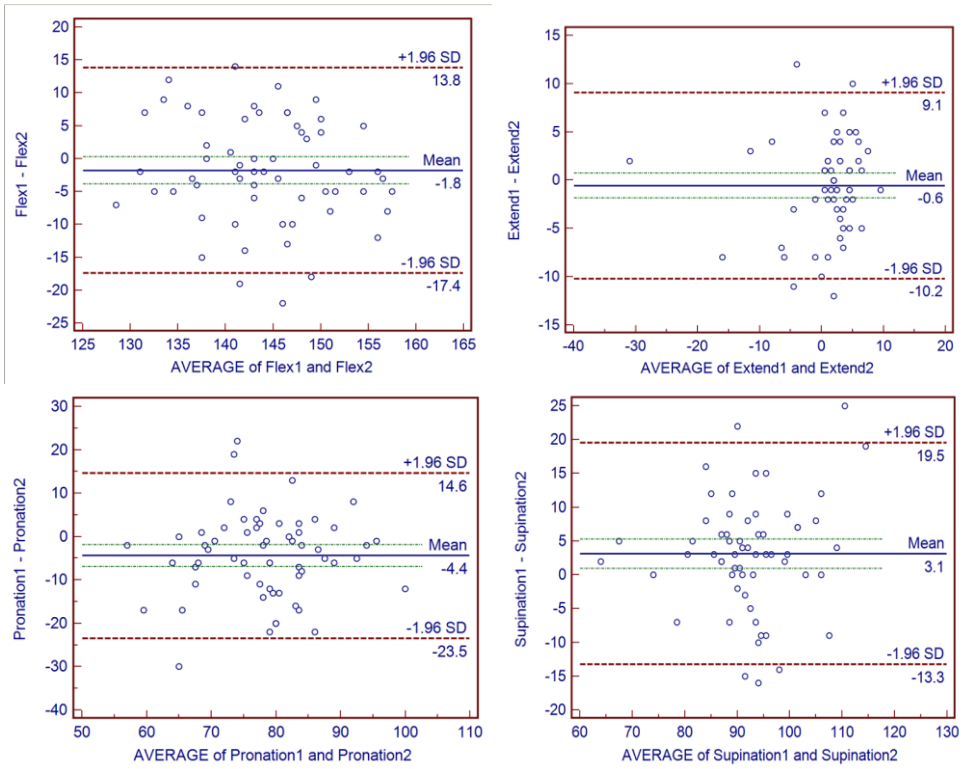


Fig. 2 Part 1 Bland-Altman analysis of inter-rater, intra-method reliability

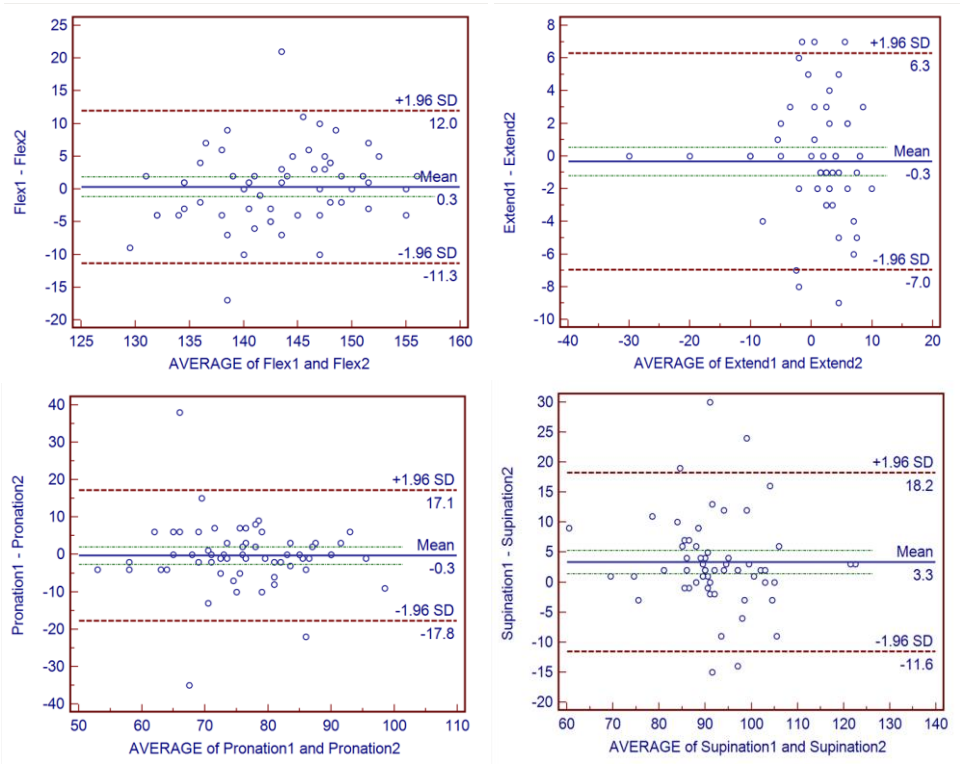


Fig. 3 Part 2 Bland-Altman analysis of intra-rater, intra-method reliability

Table 4 The percentage of range of motions within the upper limit of agreement at 10 degrees

Motion	**Part 1** Inter-rater , Intra-method	**Part 2** Intra-rater , Intra-method
Flexion	83%	95%
Extension	95%	100%
Pronation	68%	82%
Supination	78%	93%

Discussion

Part 1 is a comparison of inter-rater, intra-method reliability that determines the generalizability. It showed a good correlation in elbow extension and forearm supination. Although the others showed only fair correlation, the percentage of range of motion within the upper limit of 10 degrees was high. Although we could not conclude that this technique is generalizable, it might be possible if we could eliminate the cause of forearm rotation measurements error as described below.

Part 2 is a comparison of intra-rater, intra-method reliability by a specialist in elbow surgery in separate session. We could conclude that this technique was reproducible because it still showed a good to excellent outcome.

In addition, the interpretation of the measurement angle for each motion is different. The difference in the angle of elbow extension is less than that of the flexion or forearm rotation. From our results, the lower to upper limit of variation interval for a measurement of elbow extension was lower than elbow flexion and forearm rotation. This would suggest the error component of extension measurements was the lowest and the most reliable.

The forearm rotation measurement error could be due to many reasons. First, the measurement error might be the position of the camera because we used a camera in a constant position for subjects of different heights. We should adjust the height to be suitable with patient's height to correct the angle of recording for all subjects. The second possible explanation is likely to be the patient positioning. We did not control the shoulder level of the subject to be the same; therefore measurements of forearm rotation might be influenced by external or internal rotation of the shoulder. Patients should be positioned with their backs against a wall; this could eliminate the problem of shoulder rotation. These changes might reduce the error component of forearm rotation results.

Conclusion

The VDO clip-based goniometry method for measuring the range of motion of the elbow was reliable, generalizable and reproducible. This offers a great opportunity to follow-up the outcome assessments of patients for whom transportation to a tertiary care center is a significant barrier.

Acknowledgements

This research has financial support from Faculty of Medicine, Srinakarinwirot University.

References

1. Dhurjaty S. The economics of telerehabilitation. Telemed J E Health 2004; 10: 196-9.
2. Shafqat S, Kvedar JC, Guanci MM, Chang Y, Schwamm LH. Role for telemedicine in acute stroke. Feasibility and reliability of remote administration of the NIH stroke scale. Stroke 1999; 30: 2141-5.
3. Engbers L, Bloo H, Kleissen R, Spoelstra J, Vollenbroek-Hutten M. Development of a teleconsultation system for communication between physiotherapists concerning children with complex movement and postural disorders. J Telemed Telecare 2003; 9: 339-43.
4. Mielonen ML, Ohinmaa A, Moring J, Isohanni M. Psychiatric inpatient care planning via telemedicine. J Telemed Telecare 2000; 6: 152-7.
5. Blonna D, Zarkadas PC, Fitzsimmons JS, O'Driscoll SW. Validation of photograph-based goniometric measuring joint range of motion. J Shoulder Elbow Surg 2012; 21: 29-35.
6. Chanlalit C, Kongmalai P. Validation of the Telemedicine-Based goniometry for measuring elbow range of motion. J Med Assoc Thai 2012; 95 Suppl 12: S113-7.
7. Donner A, Elraszrw M. Sample size requirements for reliability studies. Stat Med 1987; 6: 441-8.
8. Bland JM, Altman DG. Measuring agreement in method comparison studies. Stat Methods Med Res 1999; 8: 135-60.
9. Bland JM, Altman DG. Comparing methods of measurement: why plotting difference against 247 standard method is misleading. Lancet 1995; 346: 1085-7.
10. Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of 249 clinical measurement. Lancet 1986; 1: 307-10.
11. Shrout PE, Fleiss JL. Intraclass correlations: uses in assessing rater reliability. Psychol Bull 1979; 86: 420-8.

ความน่าเชื่อถือของการวัดพิสัยการเคลื่อนไหวข้อศอกด้วยภาพจากวีดิโอคลิป

พิงควรรศ คงมาลัย, พบ, อรุณวงศ์ เทพชาตรี, พบ, ชลวิช จันทร์ลลิต, พบ

วัตถุประสงค์: *เพื่อเปรียบเทียบความน่าเชื่อถือของการใช้ภาพจากวีดิโอคลิป (VDO-clip) ในการวัดพิสัยการเคลื่อนไหวข้อศอก*

วิธีการศึกษา: *เป็นการศึกษาตัดขวาง (cross-sectional) โดยวัดพิสัยการเคลื่อนไหวข้อศอก คือการงอ เหยียด และพลิกคว่ำหงาย ของกลุ่มตัวอย่าง 30 ราย ทำต่อเนื่องจากการวิจัยเดิมที่พบว่าการวัดพิสัยโดยแพทย์ผู้เชี่ยวชาญทางข้อศอกจากการตรวจร่างกายเปรียบเทียบกับการวัดจาก VDO-clip (intra-rater/inter-method reliability) มีความถูกต้องเพียงพอ โดยงานวิจัยนี้ศึกษาในเรื่องของการวัดพิสัยการเคลื่อนไหวข้อศอกโดยเปรียบเทียบระหว่างแพทย์ผู้เชี่ยวชาญทางข้อศอกจากการตรวจร่างกายกับแพทย์ประจำบ้านออร์โธปิดิกส์จาก VDO-clip (inter-rater/intra-method reliability) และโดยแพทย์ผู้เชี่ยวชาญทางข้อศอกจาก VDO-clip ที่เวลาแตกต่างกัน (intra-rater/intra-method reliability)*

ผลการศึกษา: *ผล intraclass correlation coefficient และ Bland-Altman analysis แสดงความเป็นไปได้ในการวัดพิสัยการเคลื่อนไหวข้อศอกโดยใช้ภาพจาก VDO clip แม้ผู้วัดจะมีประสบการณ์ที่แตกต่างกันและการศึกษาสามารถวัดซ้ำที่ระยะเวลาต่างกันโดยแพทย์ผู้เชี่ยวชาญทางข้อศอกได้โดยไม่เปลี่ยนแปลงผลการศึกษา*

สรุป: *การประเมินพิสัยการเคลื่อนไหวข้อศอกด้วยภาพจาก VDO-clip โดยแพทย์ผู้เชี่ยวชาญทางข้อศอกมีความน่าเชื่อถือเพียงพอ ถึงแม้ทำซ้ำที่ระยะเวลาแตกต่างกัน ซึ่งน่าจะเป็นประโยชน์สำหรับการติดตามการรักษาของผู้ป่วยอย่างต่อเนื่อง โดยเฉพาะอย่างยิ่งผู้ป่วยที่ประสบปัญหาในการเดินทางมาโรงพยาบาล*

Comparison of Needle Aspiration and Arthrotomy Treatment for Septic Knee Arthritis: A 10-year retrospective study

Chote Pawasuttikul, MD

Department of Orthopaedics, Sawanpracharak Hospital, Nakhon Sawan, Thailand

Purpose: *There are many methods of treatment for septic arthritis employed nowadays; including serial needle aspiration, arthrotomy and debridement and arthroscopic debridement. However, there is no study of comparison between serial needle aspiration and arthrotomy treatment for septic knee arthritis. The objective of this study was to compare the results of serial needle aspiration with arthrotomy and debridement in septic knee arthritis patients.*

Methods: *Retrospective analysis of 128 cases of septic knee arthritis from January 2003 to December 2012 was performed. The 74 septic knee arthritis patients were divided into 2 groups: group I (44) were treated with serial needle aspiration and group II (30) were treated with arthrotomy and debridement. Both groups were compared by the duration of treatment and clinical results.*

Results: *The etiologies of septic knee arthritis were hematogenous infection 75%, traumatic articular wound 23%, hospital acquired infection 2% and no postoperative knee infection. There were significantly higher uses of parenteral antibiotic therapy in the aspiration group compared with the arthrotomy group ($P<0.04$). There was no significant difference in the number of complete recoveries the length of stay in hospital, the number of readmission cases due to recurrence of infection and the number of changes of management to the arthrotomy between the two groups. However, the number of readmissions and changes of management in the aspiration group were greater than the arthrotomy group (aspiration group 8.10% and 8.10% arthrotomy group 0% and 0% respectively).*

Conclusion: *In the treatment of uncomplicated septic knee arthritis, serial needle aspiration was not statistically different form arthrotomy and debridement.*

Keywords: *Arthrotomy, needle aspiration, septic knee arthritis*

The Thai Journal of Orthopaedic Surgery: 37 No.2-4: 29-33
Full text. e journal: *http://www.rcost.or.th, http://thailand.digitaljournals.org/index.php/JRCOST*

Introduction

Septic arthritis is the most rapidly destructive joint disease. The most commonly affected joint is the knee, which accounts for approximately 50% of cases, and 5-20% of the mortality rate[1]. Many medical and surgical treatments have been proposed: systemic antibiotic treatment combined with serial needle aspiration, arthrotomy with articular debridement or synovectomy, arthroscopic debridement and arthroscopic debridement with continuous irrigation suction[2]. The indications of these treatments are not well defined[3]. Some authors suggest that aspiration should only be performed in the early stages[4]. Although it has been reported that surgical treatment for septic arthritis was not superior to medical treatment, a comparison of two techniques for septic knee arthritis has not been performed[3,5,6]. The objective of this retrospective study was to compare the results of the serial needle aspiration with arthrotomy and debridment in adult patients at Sawanpracharak Hospital, Nakhon Sawan, Thailand.

Correspondence to: Pawasuttikul C, Department of Orthopaedics, Sawanpracharak Hospital, NakhonSawan, Thailand
E-mail: chote2chote@gmail.com

Patients and methods

This study is a retrospective, descriptive study. Medical records for septic knee arthritis ICD-10 [International Classification of Diseases, Tenth Revision] codes M0095 to M0097 from January 2003 to December 2012 were searched. Patients aged over 15 years presenting with septic knee arthritis were included. A knee joint was defined as septic if a culture of the joint fluid was positive, or if purulent material was found in the joint. Group I was initially treated with serial needle aspiration and group II was initially treated with arthrotomy and debridement. The inclusion criteria of both groups were patients who received treatment within 7 days form first clinical symptoms, well controlled diabetes mellitus and hypertension, no associated severe systemic disease and a complete in-patient medical record. Exclusion criteria were osteomyelitis of the distal

femur or proximal tibia, total knee arthroplasty, poorly controlled diabetes mellitus and hypertension, associated severe systemic diseases (rheumatoid arthritis, systemic lupus erythematosus (SLE), human immunodeficiency virus (HIV) infection, steroid used, old cardiovascular disease, chronic kidney disease, chronic liver disease, heart disease or carcinoma) and missing data.

Medical records were reviewed for age, gender, side of knee, pre-existing joint diseases (osteoarthritis, rheumatoid arthritis), preexisting risk factors (diabetes mellitus, hypertension, and systemic disease), etiology of the infection, duration between the first clinical symptoms and starting treatment in the hospital, blood test results [white blood cell count, C-reactive protein (CRP), and erythrocyte sedimentation rate (ESR)], radiological evidence of osteoarthritis, causative organisms, times of repeat procedures, functional status at the time of discharge from the hospital and duration of hospital stay.

Successful treatment was defined as complete resolution of the inflammatory symptoms: pain and swollen knee had subsided, absence of fever, decrease of ESR and CRP and partial weight bearing with walking aids. Unsuccessful treatment was defined as dead, readmission and change of management from repeated needle aspiration to arthrotomy. The indication to switch form aspiration to arthrotomy was no improvement of clinical signs: fever is high 48 hours after aspiration and no decrease in white blood cell count in the last synovial fluid examination. All patients were followed for a minimal period of 3-6 months.

The data were analyzed by descriptive statistical analysis; discrete data were present in frequency and percentage and continuous data were present in mean and standard deviation. The base line characteristics and the results of treatment between groups were compared by Chi square test and Fisher's exact test for discrete data and Student's *t*-test for continuous data with a statistic significance at $P<0.05$.

Results

There were 319 septic arthritis patients treated in Sawanpracharak hospital from January 2003 to December 2012 and 238 (75%) patients had complete data and medical records. One hundred and twenty eight (54%) had septic knee arthritis and 110 patients (46%) had septic arthritis of other joints. Of the 128 included patients, 74 were compatible with inclusion criteria, 52 were compatible with exclusion criteria and 2 died before any procedure was performed. The demographic data of cases are shown in Table 1. The etiologies of the septic knee arthritis were hematogenous infection 75%, traumatic articular wound 23 %, hospital acquired infection 2% and no postoperative knee infection.

There was no statistically significant difference in age, sex, side of knee, preexisting diseases, white blood cell count in synovial fluid and bacterial isolates. The comparison between the two groups revealed that the mean symptom duration times before treatment (days) was significantly shorter in the aspiration group than in the arthrotomy group ($P<0.048$) but the use of parenteral antibiotic therapy was significantly higher in the aspiration group compared to the arthrotomy group ($P<0.04$). Mean ESR levels and mean CRP levels could not been shown because of incomplete data.

The outcome of patients with septic knee arthritis based on treatment is shown in table 2. There were no statistically signicant differences in complete recovery time and the length of stay in hospital in both groups. For the readmission due to the recurrence of infection and change of management to arthrotomy, there was no statistically significant difference between both groups. However, the number of readmissions and changes of management to arthrotomy in aspiration group tend to be greater than those in arthrotomy group (aspiration group 8.10% and 8.10% arthrotomy group 0% and 0%, respectively).

Discussion

Successful treatment of a septic arthritis is the removal of purulent material form the joint either surgically or by serial needle aspiration. There is still controversy over which mode of drainage should be performed[6]. If initially treated with needle aspiration the vast majority of the purulent fluid can be removed if a joint infection is easily accessible[7], and repeated needle aspiration for recurrent joint effusions has been used with success during the first 7 days of treatment[8]. Therefore, this study set an inclusion criterion timing of seven days.

The infection staging by Gächter was most commonly used[8]. Stage I–III infections should be treated with arthroscopic joint decompression with irrigation and debridement, for stage IV infections, arthrotomy is suggested[9,10,11]. This study did not identify the infection staging because most cases were treated under emergency conditions where the arthroscopic setting is not available. The choice of treatment was influenced by the overall health of the patients including comorbidities. The present study excluded cases with comorbidities for the comparative homogenous group of patients.

In the previous studies on the outcomes of the treatment of septic knee arthritis[3,4,12], patients were heterogenous and immediate results at the time of discharge (length of stay and functional score) and long term results (osteoarthritis) were usually reported. This study sets exclusion criteria for homogenous of the patients and evaluated both immediate and intermediate outcomes (readmission).

The results of the previous study, which directly compared the outcome of native joint septic arthritis in patients treated by arthrotomy and serial needle aspiration showed no significant difference[4,5]. The results of the present study, of only septic knee arthritis, also showed no statistically significant difference in length of stay, the number of complete recoveries and the number of deaths, but when compared with the number of readmissions and the number of changes form aspiration to arthrotomy between two groups, the aspiration group was more likely to have a poor outcome. Nevertheless, these differences did not reach statistical significance.

The weakness of this study is that it is not a non-randomized controlled trial study and it has some limitations (a small number of cases, incomplete data for evaluated outcome by Bussiere functional score, or Lysholm scoring system)[13]. A prospective randomized controlled trial will be needed for further studies.

Table 1 Demographic data of septic knee arthritis patients

Characteristics	Aspiration (n=44)	Arthrotomy (n=30)	*P*-value
Age (years), mean (SD)	63.3 (11.8)	56.9 (15.9)	0.085
Sex: Male (%)	25 (56.8%)	15 (50.0%)	0.320
Female (%)	19 (43.2%)	15 (50.0%)	
Symptom duration before treatment (days)	3.9 (2.9)	5.4 (2.7)	0.048*
Side : Right	20	14	0.34
Left	18	14	
Both	8	2	
Preexisting disease			0.075
None	8	6	
Osteoarthritis	17	11	
Hypertension	12	3	
Diabetes	4	2	
Others: urinary tract infection, peptic ulcer, dyslipidemia, asthma, gouty arthritis, chronic obstructive pulmonary disease, glucose-6-phosphate dehydrogenase deficiency	10	10	
White blood cell count in synovial fluid, mean (SD)	67,149.69 (25,269.5)	62,568.5 (30,498.6)	0.537
Bacterial isolates (%)			0.20
Staphylococcus aureus sensitive to methicillin	13 (29.5%)	10 (33.3%)	
Staphylococcus aureus resistance to methicillin	3 (0.06%)	1 (3.3%)	
Streptococcus	5 (11.4%)	4 (13.3%)	
Gram negative pathogens	2 (0.05%)	3 (10.0%)	
Mixed bacterial infection	5 (11.4%)	2 (6.6%)	
No bacterial growth	16 (47.6%)	10 (33.3%)	
Antibiotic therapy : 1st regimen (cefazolin or ceftriaxone)	31	24	0.04*
2nd regimen (combine two antibiotics)	13	6	

Table 2 Outcome of septic knee arthritis patients based on treatment

Outcome	Aspiration (n=44)	Arthrotomy (n=30)	*P*-value
Length of stay, mean (SD)	10.5 (5.8)	12.5 (7.6)	0.62
Complete recovery (%)	32 (43.2%)	27 (36.5%)	0.084
Readmission (%)	6 (8.1%)	(0%)	0.075
Change form aspiration to arthrotomy (%)	6 (8.1%)	(0%)	0.075
Death (%)	5 (6.8%)	3(4.1%)	0.584

Conclusion

By comparing serial needle aspiration and arthrotomy and debridement in the treatment of septic knee arthritis in uncomplicated patients, there was no significant difference in the number of complete recoveries, the length of stay in hospital, number of readmissions, number of changes of treatment and mortality rate.

Acknowledgements

The authors would like to thank Mrs. Darika Tarnbuasawan for the statistical data analysis and would particularly like to acknowledge Dr. Mondakan Oprasertsawat, who was a research consultant and participated in the study. We also thank Dr. Pimpet Sukumalpaiboon for technical assistance on reviewing the manuscript.

References

1. Carpenter CR, Schuur JD, Everett WW, Pines JM. Evidence-based diagnostics: adult septic arthritis. Academic Emergency Medicine 2011; 18: 781-96.
2. Mathews CJ, Weston VC, Jones A, Field M, Coakley G. Bacterial septic arthritis in adults. Lancet 2010; 375: 846-55.
3. Ravindran V, Logan I, Bourke BE. Medical vs surgical treatment for the native joint in septic arthritis: a 6-year, single UK academic centre experience. Rheumatology (Oxford) 2009; 48: 1320-2.
4. Balabaud L, Gaudias J, Boeri C, Jenny JY, Kehr P. Results of treatment of septic knee arthritis: a retrospective series of 40 cases. Knee Surg Sports Traumatology Arthroscopy 2007; 15: 387-92.
5. Goldenberg DL, Brandt KD, Cohen AS, Cathcart ES. Treatment of septic arthritis comparison of needle aspiration and surgery as initial modes of joint drainage. Arthritis Rheum 1975; 18: 83-90.
6. Mathews CJ, Kingsley G, Field M, Jones A, Weston VC, Phillips M, et al. Management of septic arthritis: a systematic review. Annal of Rheumatic Disease 2007; 66: 440-5.
7. Shirtliff ME, Mader JT. Acute septic arthritis.Clinical microbiology reviews 2002; 15: 527-44.
8. Gächter A. Arthroscopic lavage for joint infections. Orthopaedaedics Traumatology 1993; 2: 104-6.
9. Ateschrang A, Albrecht D, Schroeter S, Weise K, Dolderer J. Current concepts review: septic arthritis of the knee pathophysiology, diagnostics, and therapy. Wien Klin Wochenschr 2011; 123: 191-7.
10. Wirtz DC, Marth M, Miltner O, Schneider U, Zilkens KW. Septic arthritis of the knee in adults: treatment by arthroscopy or arthrotomy. Int Orthop 2001; 25: 239-41.
11. Kuo CL, Chang JH, Wu CC, Shen PH, Wang CC, Lin LC, et al. Treatment of septic knee arthritis: comparison of arthroscopic debridement alone or combined with continuous closed irrigation-suction system. J Trauma 2011; 71: 454-9.
12. Chen CM, Lin HH, Hung SC, Huang TF, Chen WM, liu CL, et al. Surgical treatment for septic arthritis of the knee joint in elderly patients: a 10-year retrospective clinical study. J Orthopedics. 2013; 36: 434-43.
13. Yanmis I, Oskan H, Koca K, Kilincoqlu V, Bek D, Tunay S. The relation between the arthroscopic findings and functional outcomes in patients with septic arthritis of the knee joint, treated with arthroscopic debridement and irrigation. Acta Orthopaedics Traumatology Turc 2011; 45: 94-9.

ผลการรักษาโรคข้อเข่าอักเสบติดเชื้อโดยการเจาะดูดจากข้อเปรียบเทียบกับการผ่าตัดเปิดล้างข้อ: การศึกษาย้อนหลัง 10 ปี

โชติ ภาวศุทธิกุล, พบ

วัตถุประสงค์: *การรักษาโรคข้ออักเสบติดเชื้อมีหลายวิธี วิธีที่นิยมปฏิบัติได้แก่ การเจาะดูดจากข้อ การผ่าตัดเจาะข้อ การผ่าตัดเปิดล้างข้อ ที่ผ่านมายังไม่มีการศึกษาผลการรักษาโรคข้ออักเสบติดเชื้อเฉพาะข้อเข่าโดยการเจาะดูดจากข้อเปรียบเทียบกับการผ่าตัดเปิดล้างข้อ วัตถุประสงค์ของการศึกษานี้เพื่อเปรียบเทียบ ผลการรักษาข้อเข่าอักเสบติดเชื้อ โดยการเจาะดูดจากข้อกับการผ่าตัดเปิดล้างข้อ*

วิธีการศึกษา: *ศึกษาย้อนหลังแบบพรรณนาในผู้ป่วยที่เข้ารับการรักษาในโรงพยาบาลสวรรค์ประชารักษ์ ด้วยโรคข้อเข่าอักเสบติดเชื้อตั้งแต่วันที่ 1 มกราคม 2546 ถึง วันที่ 31 ธันวาคม 2555 เกณฑ์ในการคัดเลือกผู้ป่วยเข้าศึกษา ได้แก่ ผู้ป่วยที่เข้ารับการรักษาภายใน 7 วันหลังจากเริ่มมีอาการ มีโรคเบาหวาน หรือโรคความดันโลหิตสูงร่วมด้วยแต่ควบคุมได้ดี ไม่มีโรคเรื้อรังที่รุนแรง และ มีข้อมูลในเวชระเบียนครบถ้วนสมบูรณ์ เกณฑ์ในการคัดเลือกผู้ป่วยออก ได้แก่ การติดเชื้อที่กระดูกร่วมด้วย การผ่าตัดใส่ข้อเข่าเทียม โรคเบาหวานและโรคความดันโลหิตสูงที่ควบคุมไม่ได้ โรคเรื้อรังที่มีอาการรุนแรงต่างๆร่วมด้วย ได้แก่ โรคข้ออักเสบรูมาตอยด์ โรคเอสแอลอี โรคภูมิคุ้มกันบกพร่อง การใช้ยาเสตียรอยด์ โรคหลอดเลือดสมอง โรคไตวายเรื้อรัง โรคตับเรื้อรัง โรคหัวใจ โรคมะเร็ง เป็นต้น รวมทั้งผู้ป่วยที่มีข้อมูลไม่ครบถ้วน โดยรวบรวมผู้ป่วยที่เข้าได้กับข้อบ่งชี้ทั้งหมด 74 ราย จากผู้ป่วยข้อเข่าอักเสบติดเชื้อทั้งหมด 128 ราย กลุ่มที่ 1 รักษาด้วยการเจาะดูดหนองในข้อ 44 ราย กลุ่มที่ 2 รักษาด้วยการผ่าตัดเปิดล้างข้อ 30 ราย เปรียบเทียบการรักษาระหว่าง 2 กลุ่ม ในเรื่องระยะเวลานอนในโรงพยาบาล และผลการรักษา*

ผลการศึกษา: *พบสาเหตุของข้อเข่าอักเสบติดเชื้อจากการติดเชื้อในกระแสเลือดร้อยละ 75 การบาดเจ็บที่ข้อเข่าร้อยละ 23 การติดเชื้อภายในโรงพยาบาลร้อยละ 2 การใช้ยาปฏิชีวนะในกลุ่มเจาะดูดหนองมากกว่าในกลุ่มผ่าตัดเปิดล้างข้ออย่างมีนัยสำคัญทางสถิติ ในขณะที่ระยะเวลานอนโรงพยาบาล และจำนวนผู้ป่วยที่หายเป็นปกติ จำนวนผู้ป่วยที่เสียชีวิตของทั้งสองกลุ่มไม่แตกต่างกัน สำหรับจำนวนผู้ป่วยที่ติดเชื้อซ้ำจนต้องเข้ารับการรักษาใหม่ และจำนวนผู้ป่วยที่ต้องเปลี่ยนการรักษาจากการเจาะดูดหนองไปเป็นการผ่าตัดเปิดล้างข้อเข่า ในกลุ่มที่ 1 มีแนวโน้มสูงกว่ากลุ่มที่ 2 แต่เมื่อวิเคราะห์ทางสถิติแล้วพบว่าไม่มีความแตกต่างกัน*

สรุป: *การรักษาผู้ป่วยโรคข้อเข่าอักเสบติดเชื้อที่ไม่ซับซ้อน โดยการเจาะดูดหนองในข้อเข่าเปรียบเทียบกับการผ่าตัดเปิดล้างข้อให้ผลการรักษาไม่แตกต่างกัน ทั้งในเรื่องระยะเวลานอนในโรงพยาบาล จำนวนผู้ป่วยที่หายเป็นปกติ จำนวนผู้ป่วยที่ติดเชื้อซ้ำจนต้องเข้ารับการรักษาใหม่ จำนวนผู้ป่วยที่ต้องเปลี่ยนแปลงการรักษาจากการเจาะดูดหนองไปเป็นการผ่าตัดล้างข้อเข่า และจำนวนผู้ป่วยที่เสียชีวิต*

Comparison between Open Reduction and Internal Fixation and Minimally Invasive Plate Osteosynthesis for Treatment of Distal Tibia Fractures

Nuttaphan Kiriwichian, MD

Division of Orthopaedics, Nakhonpathom Hospital, Nakhonpathom, Thailand

Purpose: *To compare the results of distal tibia fractures treated by open reduction and internal fixation (ORIF) with minimally invasive plate osteosynthesis (MIPO).*
Methods: *A prospective randomized controlled study of 36 patients with distal tibia fractures (Type A, AO/OTA classification) in Nakhonpathom Hospital from May, 2011 to February, 2013. These patients were diagnosed as closed fracture or open fracture grade I by Gustilo classification. Twenty one were treated by ORIF and fifteen were treated by MIPO using distal tibia locking plate. The operating time, bone union time, rates of superficial infection, rates of malunion and delayed union, and functional outcome according to Teeny and Wiss criteria were analyzed at a 6-month follow-up.*
Results: *Operating time, bone union time, functional outcome, rates of superficial infection were not significantly different between both groups. No malunion and delayed union were observed in either group.*
Conclusion: *The results of distal tibia fractures treated by ORIF with MIPO were not significantly different.*

Keywords: *Distal tibia fractures, ORIF, MIPO, infection rate, functional outcome*

The Thai Journal of Orthopaedic Surgery: 37 No.2-4: 35-41
Full text. e journal: *http://www.rcost.or.th, http://thailand.digitaljournals.org/index.php/JRCOST*

Introduction

The treatment of a distal tibia fracture is still challenging because of high complication rates such as soft tissue problems, infection, osteomyelitis, delayed union, malunion and secondary osteoarthritis of the ankle.

According to the classification of distal tibia fracture (AO/OTA)[1], there are three types:

Type A: Extra-articular distal tibia fracture

Type B: Partial articular fracture

Type C: Complete metaphyseal fracture with articular involvement

The distal tibia fractures have been treated by a variety of methods, including plaster immobilization, traction, open reduction and internal fixation (ORIF) with plates, closed intramedullary, minimally invasive plate osteosynthesis (MIPO), and external fixation.

Ruedi and Allgower reported good to excellent results in 70 of 75 distal tibia fractured patients treated by open reduction and internal fixation with plates in 1960-1970[2].

MIPO technique was a new technique and used biological fixation principle[3]. The indications were periarticular fracture, metaphyseal fracture, diaphyseal fracture where intramedullary nailing was not indicated[4-8].

Correspondence to: Kiriwichian N, Division of Orthopaedics, Nakhonpathom Hospital, Nakhonpathom, Thailand
E-mail: nuttaphan_nph@hotmail.com

Helfet et al. reported the results of distal tibia fractures treated by MIPO[9]. There was no loss of fixation or evidence of hardware fracture. Twenty distal tibia fractures were union but delayed union, deformity, and superficial cellulitis were reported.

The objective of this study was to compare the results of distal tibia fractures treated by ORIF and MIPO in Nakhonpathom Hospital.

Patients and Methods

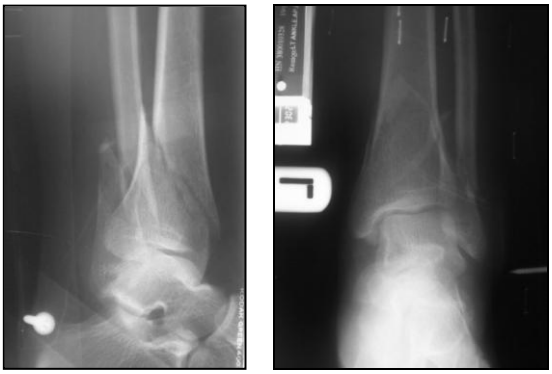
A prospective randomized controlled study compared 36 patients with extra-articular distal tibia fracture (type A, AO/OTA classification) in Nakhonpathom Hospital from May, 2011 to February, 2013. The study was approved by the ethical committee of Nakhonpathom Hospital. These patients were diagnosed with a closed fracture or open fracture grade I by Gustilo classification. Twenty one distal tibia fractures were treated by ORIF and fifteen were treated by MIPO. The associated injury, routine pre-anesthetic investigation, standard anteroposterior and lateral radiographs of the ankle joint which included the tibia were recorded (Fig. 1).

Closed fractures or open fractures of distal tibia grade I by Gustilo classification (type A1, A2, A3, AO/OTA classification) were included in this study. Patients with distal tibia fractures (type B, C, AO/OTA classification), open fractures of the distal tibia grade II and III by Gustilo classification, multiple fractures, uncontrolled diabetes or vascular

diseases were excluded. Informed consent was obtained from the patients.

The patients with closed fracture were treated by anti-edema drug for 5-7 days until the skin was wrinkled. Preoperative antibiotics (first-generation cephalosporin) were administered 30 minutes before the operation.

The patients with an open fracture were debrided in the first operation and initially stabilized with a long leg slab. Postoperative management included anti-edema drug and first generation cephalosporin for 5-7 days until they no longer had symptoms and signs of infection. Then the second operation was performed.



A B

Fig. 1 A 40-year-old man who sustained an injury from a motorcycle accident with an extra articular distal tibia fracture. Preoperative anteroposterior (A) and lateral (B) radiographs

Surgical technique

Under a tourniquet, the fibula was fixed firstly by open reduction and internal fixation with a one-third tubular plate and followed by the tibia.

In ORIF group, the standard anteromedial approach was performed. The distal tibia fracture was fixed to a distal tibia locking plate with at least 3 screws for each main fragment. On postoperative day1, the patient was allowed to move ankle joint without support, and ambulation with crutches in day 2. Weight bearing was protected.

In MIPO group, the patient was supine on the radiolucent operative table. An indirect reduction technique was carried out and alignment checked by fluoroscopy (Fig. 2). A distal incision was performed at the medial site of the distal tibia. The saphenous vein and nerve were identified. A proximal incision was made under fluoroscope for at least 3 screws in the proximal fragment. A subcutaneous extraperiosteal tunnel was created and follow by the insertion of a plate from the distal to proximal incision[10,11]. The locking plate position was checked until proper positioning was achieved. Locking screws were inserted with at least 3 screws in the proximal and 3 screws in the distal fragments (Fig. 3). The postoperative program was the same as the ORIF group.

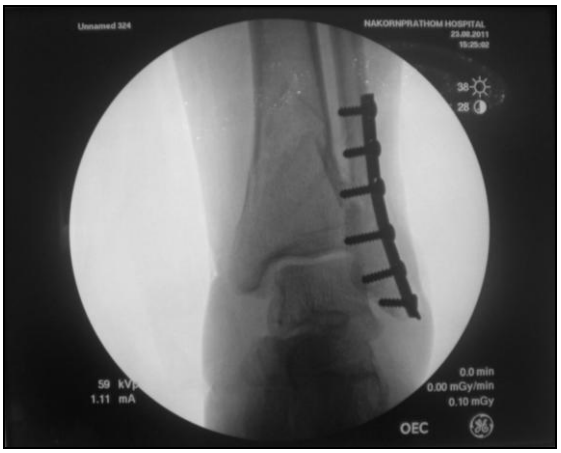


Fig. 2 The indirect reduction technique was completed and alignment checked by fluoroscopy

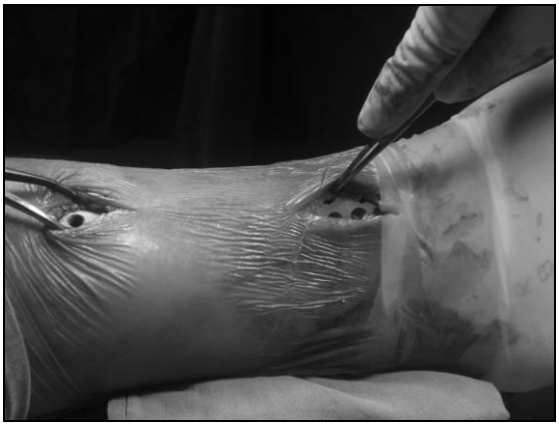
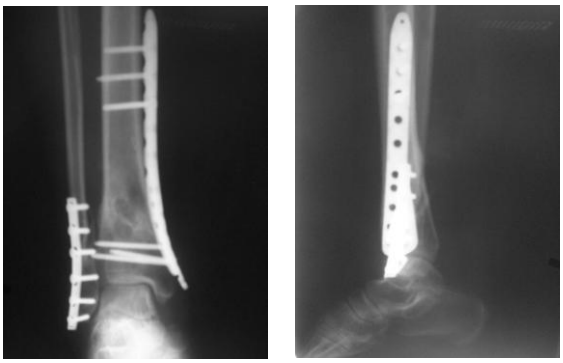


Fig. 3 The distal tibia fracture was stabilized with a locking compression plate by MIPO technique



A B

Fig. 4 Postoperative anteroposterior (A) and lateral (B) radiographs at 3 months demonstrated complete bone healing

The patient was scheduled for follow-ups every 4 weeks until the fracture united. Wound condition and range of motion of ankle were evaluated and a radiograph of distal tibia was taken. Fracture healing was defined as radiological evidence of bridging mature callus at least three cortices as seen in both anteroposterior and lateral radiographs (Fig. 4). The functional outcome was evaluated with the clinical rating system for the ankle by Teeny and Wiss criteria[12] at a 6 months follow-up (Table 1). All patients took calcium 1,250 mg/day and alfacalcidol 0.25 μg/day. The data were analyzed by the Mann-Whitney U-test and Fisher's exact test.

Table 1 Teeny and Wiss criteria (symptoms and functional evaluation of ankle)

Parameters	Points
1. Pain	
a) No pain, including long walks, running or sports.	50
b) Slight or occasional pain, pain after long walk or sports, or mild pain at end of day.	45
c) Mild pain with walking or running, but no change in activities of daily living. May have some pain going up or down stairs or walking on uneven ground. May require non-narcotic pain medicine several times a week.	40
d) Mild-moderate pain, tolerable, but requires some concessions to pain. May required daily non-narcotic pain medicine. No night pain.	30
e) Moderate pain. Definite change in activities of daily living, pain at rest or at night, despite restriction of activities. Occasional weak narcotic needed.	20
f) Continuous pain, regardless of activities, most often not relieved with non-narcotic medication. Dependent on narcotic pain medicine for significant pain relief. Severe limitations of activities.	10
g) Disabled because of pain. Constant pain, no relief with medicines.	0
2. Distance	
a) Unlimited	8
b) Limited, but greater than 6 blocks	6
c) 4-6 blocks	4
d) 1-3 blocks	2
e) Indoors only	1
f) Bed-chair, or unable to walk.	0
3. Supports or Orthosis	
a) None	8
b) Soft wrap needed for long walk	7
c) Cane or orthosis, only for long walks	6
d) Cane, single crutch or orthosis full time	4
e) Two canes or two crutches	2
f) Walker or unable to walk	0
4. Running	
a) Unlimited, as such as desired	5
b) Limited, but able to run	3
c) Unable to run	0

5. Toe raising	
a) Able to raise on toes x 10 repetitions	5
b) Able to raise on toes x 5 repetitions	3
c) Able to raise on toes x 1 repetitions	1
d) Unable to raise on toes	0
6. Hills (up or down)	
a) Up and down normally	3
b) Climbs and /or descends with foot externally rotated	2
c) Climbs and/or descends on toes or by side stepping	1
d) Unable to climb and/or descend hills	0
7. Stairs (up or down)	
a) Climbs and descends normally	3
b) Needs banister	2
c) Steps down and/or up with normal foot only	1
8. Limp	
a) None	8
b) Only when fatigued	6
c) Slight, constant	4
d) Moderate, constant	2
e) Marked	0
9. Swelling	
a) None	3
b) Only in the evening or after walking	2
c) Constant, mild (less than 1 cm difference around calf)	1
d) Marked	0
10. Plantar range of motion	
a) Greater than 30°	2
b) Greater than 10°	1
c) Less than 10°, or presence of equines contracture	0
11. Dorsal range of motion	
a) Greater than or equal to 15°	5
b) Greater than or equal to 10°, less than 15°	4
c) Greater than or equal to 0°, less than 10°	3

Results

There were 36 distal tibia fractures with 30 closed fractures and 6 open fractures grade 1 by Gustilo classification. There were 18 males and 18 females.

There were 21 patients in the ORIF group. There were 12 males (57.0%), 9 females (43.0%) and 15 close fractures (71.0%), 6 open fractures (29.0%). The mean age was 48.5 years (range 30-66 years). The superficial wound infection rate was 28.6% (6 in 21).

There were 15 patients in the MIPO group. There were 6 males (40.0%), 9 female (60.0%) and 15 close fractures (100%). The mean age was 41.2 years (range 17-71 years). The superficial wound infection rate was 6.7% (1 in 15).

Table 2 Clinical outcomes between ORIF and MIPO for treatment of distal tibia fractures

Results	ORIF group (n=21)			MIPO group (n=15)			Z	*P*-value*
	Mean (SD)	Min	Max	Mean (SD)	Min	Max		
Operating Time (minutes)	70.7 (9.3)	60.0	90.0	73.0 (15.2)	60.0	100.0	0.00	1.00
Bone Union Time (weeks)	12.3 (2.0)	10.0	14.0	13.2 (1.7)	10.0	14.0	-1.41	0.16
Teeny and Wiss Score	90.7 (5.0)	83.0	96.0	93.4 (1.4)	92.0	95.0	-0.59	0.55

*Mann-Whitney U-test

Malunion and delayed union were not found in either group. The clinical outcomes between ORIF and MIPO for treatment of distal tibia fractures are displayed in table 2.

Comparing the operating time, the MIPO group was not significantly different to the ORIF group (Mann-Whitney U-test, *P*=1.00).

Comparing the bony union time, the MIPO group was not significantly different to the ORIF group (Mann-Whitney U-test, *P*=0.16).

Comparing the functional outcome by the clinical rating system for the ankle (Teeny and Wiss criteria), the MIPO group was not significantly different to the ORIF group (Mann-Whitney U-test, *P*=0.55).

Comparing the superficial wound infection rate, the MIPO group was not significantly different to the ORIF group (Fisher's exact test *P*=0.20, odd ratio=5.6, 95% CI: 0.60-52.54).

Discussion

The goals of treatment of a distal tibia fracture are anatomical articular reduction, restoration of axial alignment, maintenance of joint stability, achievement of fracture union, pain free weight baring and motion, and no wound complications.

The treatment plan in a distal tibia fracture depends on fracture pattern, soft tissue injury, patient co-morbidity, fixation resources, and surgical experience.

The main disadvantage of ORIF for the distal tibia fracture is wound complication. Yih-Shiunn Lee et al. reported a superficial infection rate of 12.2% and malunion of 2% in distal tibia fracture treatment by ORIF technique[13]. However, this study showed that the superficial infection rate was higher (28.6%) and malunion rate was lower (0%) than the previous study. Superficial infections occurred in open fractures or high soft tissue injuries and was treated with oral antibiotics.

MIPO has gained popularity in treatment of long bone fractures. This biological fixation was a physiologic process of bone healing and optimally with minimal amount of soft tissue injury[14]. The indirect reduction principle of MIPO was reposition and realigning by manipulation at a distance away from the fracture site, preserving soft tissue (indirect induction technique), leaving comminuted out of the mechanical construct, while preserving their blood supply, using low elastic modulus, biocompatible materials, limited operative exposure.

Mahajan reported the MIPO technique in 20 patients with distal tibia fractures, 14 excellent, 4 good, and 2 fair results[15]. Two patients had superficial wound infection. However, our study demonstrated that the superficial infection rate was lower (6.7%) than the previous study. Good preparation of soft tissue in preoperative program can reduce superficial wound infection.

Webb et al. reported that functional outcomes following minimally invasive locking plate osteosynthesis in distal tibia fractures did not significantly differ from that of the general population[16]. In our study, the MIPO group did not have better functional outcome than the ORIF group. A lower infection rate in the MIPO group was not related to a good functional outcome. The superficial infection rate did not affect bone union time.

In our study, the operating time, bone union time, functional outcome and superficial infection rate were not significant difference in either group. One of the factors is, because, we do both techniques by caring of the soft tissue and not striping the periosteum unnecessarily, so we can avoid complications as a result of poor tissue handling. On the other hand, MIPO used indirect reduction under fluoroscopy. The disadvantage of MIPO is more radiation exposure to the operating team compared with ORIF. However, the advantage of MIPO is soft tissue preservation under treatment with skillful surgeons and may lower the risk of radiation exposure and avoid unfavorable results. Although this study had a small number of cases, a further study with a larger population will be required to obtain more information.

Conclusion

The present study demonstrated that patients treated by MIPO technique did not have better outcomes than patients treated by ORIF technique. MIPO was an alternative for the treatment of a distal tibia fracture.

Acknowledgements

The author would like to thank the director of Nakhonpathom Hospital, Assis. Prof. Wiwat Surangsrirat, Assoc. Prof. Sataya Rojanasthien, and Prof. Theerachai Apivatthakakul, Department of Orthopaedics, Faculty of Medicine, Chiangmai University for their valuable suggestions.

References

1. Whittle AP, Wood GW. Factures of lower extremity. In: Canale ST, editor. Cambell's operative orthopaedics. 10th ed. St. Louis: Mosby; 2003. p. 2725-872.
2. Marsh JL, Saltzman CL. Ankle fractures. In: Bucholz RW, Heckman JD, editor. Rockwood and green's fractures in adult V.2. 5th ed. Philadelphia: Lippincott Williams & Wilkins; 2001. p. 2001-90.
3. Gautier E, Ganz R. The biological plate osteosynthesis. Zentralbl Chir 1994; 119: 564-72.
4. Helfet DL. Suk M. Minimally invasive percutaneus plate osteosynthesis of fracture of the distal tibia. Instr Course Lect 2004; 53: 471-5.
5. Apivatthakakul T, Arpornchayanon O, Bavornratanavech S. Minimally invasive plate osteosynthesis (MIPO) of the humeral shaft fracture. Is it possible? A cadaveric study and preliminary report. Injury 2005; 36: 530-8.
6. Apivatthakakul T, Chiewcharntanakit S. Minimally invasive plate osteosynthesis (MIPO) in the treatment of the femoral shaft fracture where intrameddurary nailing is not indicated. Int Orthop 2009; 33: 1119-26.
7. Oh CW, Oh JK, Kyung HS, Jeon IH, Park BC, Min WK, et al. Double plating of unstable proximal tibial fractures using minimally invasive percutaneous osteosynthesis technique. Acta Orthop 2006; 77: 524-30.
8. Oh CW, Park BC, Kyung HS, Kim SJ, Kim HS, Lee SM, et al. Percutaneous plating for unstable tibial fractures. J Orthop Sci 2003; 8: 166-9.
9. Helfet DL, Shonnard PY, Levine D, Borrelli J Jr. Minimally invasive plate osteosynthesis of distal fractures of the tibia. Injury 1997; 28 Suppl 1: A42-7.
10. Apivattahakakul T, Khong S. Tibia KS, Shaft F. In: Tong G, Bavonratanavech S, editor. AO manual of fracture management. Minimally invasive plate osteosynthesis (MIPO). Concepts and cases presented by AO East Asia. Stuttgard New York: Georg Thieme Verlage; 2006. p. 208-302.
11. Bavonratanavech S. Instruments. In: Tong G, Bavornatanavech S, editors. AO manual of fracture management. Minimally invasive plate osteosynthesis (MIPO). Concepte and cesea presented by AO East Asia. Stuttgart New York: GeorgThieme Verlag; 2006. p. 20-9.
12. Teeny SM, Wiss DA. Open reduction and internal fixation of tibial plafond fractures. Variables contributing to poor results and complications. Clin Orthop Relat Res 1993; 292: 108-17.
13. Lee YS, Chen SH, Lin JC, Chen YO, Huang CR, Cheng CY. Surgical treatment of distal tibia fractures: a comparison of medial and lateral plating. Orthopedics 2009; 32: 163.
14. Robert WC. Principles of internal fixation. In: Bucholz RW, Heckman JD, editor. Rockwood and green's fractures in adults. 4th ed. Philadelphia: Lippincott Williams & Wilkins; 1996. p. 159-217.
15. Mahajan N. Minimally invasive techniques in Distal Tibial Fractures. JK Science 2008; 10: 78-80.
16. Webb J, Mc Murtry I, Port A, Liow R. Fractures of the distal tibia: Functional outcome following Minimally Invasive locking Plate Osteosynthesis. J Bone Joint Surg Br 2012; 94B: 90.

การเปรียบเทียบผลการรักษากระดูกหน้าแข้งส่วนปลายหักด้วยวิธีการผ่าตัดเปิดแผลมาตรฐานกับการผ่าตัดเปิดแผลเล็ก

นัทพันธุ์ คีรีวิเชียร, พบ

วัตถุประสงค์: *เปรียบเทียบผลการรักษาผู้ป่วยกระดูกหน้าแข้งส่วนปลายหักระหว่างวิธีการผ่าตัดเปิดแผลมาตรฐานกับวิธีการผ่าตัดเปิดแผลเล็ก*

วิธีการศึกษา: *ได้ทำการศึกษาแบบสุ่มตัวอย่างไปข้างหน้าโดยแบ่งผู้ป่วยกระดูกหน้าแข้งส่วนปลายหักทั้งแบบแผลปิดและแบบแผลเปิดระดับที่ 1 ออกเป็น 2 กลุ่ม โดยกลุ่มที่ 1 ใช้วิธีการผ่าตัดเปิดแผลมาตรฐาน และกลุ่มที่ 2 ใช้วิธีการผ่าตัดเปิดแผลเล็กโดยใช้อุปกรณ์ distal tibia locking plate ระยะเวลาการศึกษาตั้งแต่เดือนพฤษภาคม พ.ศ. 2554 ถึงเดือนกุมภาพันธ์ พ.ศ. 2556 ในโรงพยาบาลนครปฐมเปรียบเทียบในเรื่องของระยะเวลาในการผ่าตัด ระยะเวลาในการติดของกระดูก ผลแทรกซ้อนที่เกิดขึ้นและวัดผลลัพธ์ที่เกิดจากการใช้งานโดยอาศัย clinical rating system for the ankle ของ Teeny and Wiss criteria ที่ระยะเวลา 6 เดือนหลังการผ่าตัด*

ผลการศึกษา: *ศึกษาในผู้ป่วยทั้งหมด 36 รายแบ่งเป็นการผ่าตัดเปิดแผลมาตรฐาน 21 รายและการผ่าตัดเปิดแผลเล็ก 15 ราย พบว่าระยะเวลาการผ่าตัดของทั้งสองวิธีไม่มีความแตกต่างกัน (P=1.0) ระยะเวลาในการเชื่อมติดของกระดูกทางเอ็กซเรย์ของทั้งสองวิธีไม่มีความแตกต่างกัน (P=0.18) ผลลัพธ์จากการใช้งานจาก Teeny and Wiss criteria ของทั้งสองวิธีไม่มีความแตกต่างกัน (P=0.55) อัตราการติดเชื้อที่ผิวหนังของทั้งสองวิธีไม่มีความแตกต่างกัน (P=0.20) ผลจากการผ่าตัดทั้งสองวิธีไม่พบกระดูกติดผิดรูปและไม่พบกระดูกติดช้า*

สรุป: *การผ่าตัดเปิดแผลเล็กมีผลลัพธ์ไม่แตกต่างกันกับการผ่าตัดเปิดแผลมาตรฐานในการรักษาผู้ป่วยกระดูกหน้าแข้งส่วนปลายหัก*

Prevalence and Conditions Associated with Neuropathic Pain in Orthopaedic Patients of Bangkok Metropolitan Administration General Hospital

Somkiat Yongyingsakthaworn, MD, Natcha Kulsiriitthikorn, BNS

Department of Orthopedics, Bangkok Metropolitan Administration General Hospital, Bangkok, Thailand

Purpose: Neuropathic pain results from a primary lesion or dysfunction in the nervous system. Diagnosing neuropathic pain can be difficult, however, this condition is common in clinical practice. There is limited information on the prevalence of neuropathic pain in the Thai orthopaedic departments. The objective of this study was to investigate the prevalence of neuropathic pain and association factors in the orthopaedic out-patient clinic, Bangkok Metropolitan Administration (BMA) Hospital.
Methods: A cross-sectional study of 400 patients attending the orthopaedic out-patient clinic, BMA hospital was conducted. The Thai DN4 questionnaire was used for the diagnosis of neuropathic pain. Main diagnosis and co-morbidities were recorded. Descriptive statistics were used to provide the basic information. The Chi-square test was applied for the association and binary logistic regression was used for multivariate analysis.
Results: The prevalence of neuropathic pain was 22.3%. The missed diagnosis rate was found to be 16.2%. There was statistically significant association between neuropathic pain and nerve entrapment.The most common symptoms used in practice by physicians for the diagnosis of neuropathic pain were reported as tingling (92.1%), pins and needles (78.7%) and numbness (70.8%) in this study.
Conclusion: This study demonstrated a need to increase awareness of neuropathic pain in orthopaedic out-patient clinics. Health care providers should promote the DN4 questionnaire to diagnose neuropathic pain in clinical practice.

Keywords: Neuropathic Pain, orthopaedic, out-patient clinic

The Thai Journal of Orthopaedic Surgery: 37 No.2-4: 43-47
Full text. e journal: *http://www.rcost.or.th, http://thailand.digitaljournals.org/index.php/JRCOST*

Introduction

Neuropathic pain can be defined as "pain initiated or caused by a primary lesion or dysfunction in the nervous system"[1]. In clinical practice, neuropathic pain can be found in many conditions such as traumatic conditions, neurological diseases, post-operative conditions and cancer. The prevalence of neuropathic pain has been reported differently ranging from 6.8-48.0% depending on where the studies were performed and the associated conditions. Most of the studies were performed outside of Thailand. There is limited information on the study of the prevalence of neuropathic pain in the Thai orthopaedic department. Diagnosing neuropathic pain can be difficult, however, this condition is common in clinical practice[2-6]. Under-evaluation and inadequate treatment results in a low quality of life[7-10]. The prevalence of neuropathic pain and its association factors in the orthopaedic department are important information to improve awareness and the efficacy of treatment.

Correspondence to: Yongyingsakthaworn S, Department of Orthopedic Surgery, Bangkok Metropolitan Administration General Hospital, Bangkok, Thailand
E-mail: somkiatsi34@yahoo.com

Patients and methods

This cross-sectional descriptive study was conducted in the Department of Orthopaedics, Bangkok Metropolitan Administration General Hospital in December 2012. The present study was approved by the Ethical Committee of Bangkok Institution. The sample size estimation was calculated using the prevalence of 10% from the literature. The sample size required can be calculated according to the following formula:

$$n = \frac{Z^2_{\alpha/2} P(1-P)}{d^2}$$

n = Sample size
P = The expected prevalence value from literature reviews (0.1)
d = Acceptable margin of error (0.03)
$Z_{\alpha/2}$ = Area under normal curve corresponding to the 95% confidence level (1.96)

For a prevalence study, 385 participants were needed. Four hundred out-patient participants from the orthopaedic clinic were recruited in office hours (Monday to Friday, 9.00-16.00) by simple random sampling generated from a computer. All patients signed an informed consent form prior to

their participation in the study. Inclusion criteria were all patients who were aged above 18 years old and willing to be completely interviewed and examined. Exclusion criteria were psychiatric disorder and reattending patients. Data collection [Patients' demographic profiles, history of recent surgery, history of co-existing medical diseases and the Thai version of the DN4 questionnaire (interview part)] was performed by an orthopaedic nurse. The patients underwent a regular physical examination, diagnosis, and treatment by a randomized orthopaedic surgeon. Then, an orthopaedic nurse collected the data [main diagnosis and the DN4 questionnaire (physical examination part)]. After all the data were collected, neuropathic pain was diagnosed by a score equal or more than 4 in the Thai version of the DN4 questionnaire. This questionnaire was passed through systematic translation and validation processes[11-12].

Statistical analysis

The quantitative data were analysed by the mean values and standard deviation. Chi-square was used to test the association between two qualitative variables. Binary logistic regression was used for the analysis of multivariate data. The level of statistical significance was set at $P<0.05$.

Results

In December 2012, 3,932 patients attended the orthopaedic out-patient clinic, BMA hospital. Four hundred patients were included. One hundred and forty one (35.3%) were male and 259 (64.8%) were female. The demographic data are shown in table 1. The prevalence of neuropathic pain was 22.3% and missed diagnosis was found to be 16.2%. Most of the main diagnoses were myofascial pain, degenerative disease and nerve entrapment conditions accounting for 24.8%, 23.0% and 19.8%, respectively. Tingling (92.1%), pins and needles (78.7%), and numbness (70.8%) were the most common symptoms of neuropathic pain. Neuropathic pain characteristics are shown in table 2. The associated condition for neuropathic pain was nerve entrapment as shown in table 3.

Table 1 Characteristics of participants (n = 400)

			Neuropathic pain (n=89)	**No Neuropathic Pain (n = 311)**
Age* (years)			58.1±11.6 (19 to 88)	57.4±14.8 (19 to 89)
Sex	Female		56 (62.9%)	203 (65.3%)
	Male		33 (37.1%)	108 (34.7%)
Weight*(kg)			62.6±11.5 (39 to 98)	62.9±12.0 (35 to 99)
Height*(cm)			158.7±7.6 (140 to 171)	157.3±9.1 (135 to 180)
Main diagnosis	Traumatic condition	(i.e. fracture, tissue injury)	4 (1.0%)	44 (11.0%)
	Post-surgical condition	(only orthopaedic surgery)	14 (3.5%)	25 (6.3%)
	Tendinitis disease	(i.e. tenosynovitis)	6 (1.5%)	47 (11.8%)
	Inflammatory disease	(i.e. RA, gout)	1 (0.3%)	9 (2.3%)
	Myofascial pain		37 (9.3%)	62 (15.5%)
	Nerve entrapment	(i.e. CTS, spinal stenosis)	54 (13.5%)	25 (6.3%)
	Degenerative disease	(i.e. osteoarthritis)		
	Pain more than 6 wks		2 (0.5%)	12 (3.0%)
	Pain less than 6 wks		10 (2.5%)	68 (17.0%)
Comorbidities	Hypertension		19 (4.8%)	71 (17.8%)
	Diabetes mellitus		18 (4.5%)	33 (8.3%)
	Dyslipidemia		4 (1.0%)	32 (8.0%)
	Others		63 (15.8%)	245 (61.3%)

*The values are given as the mean ± SD with the range
CTS carpal tunnel syndrome, *RA* rheumatoid arthritis

Table 2 Neuropathic pain characteristics

Characteristics of pain	n	%
Burning	60	67.4
Painful cold	22	24.7
Electric shocks	49	55.1
Tingling	82	92.1
Pins and needles	70	78.7
Numbness	63	70.8
Itching	19	21.4
Hypoesthesia to touch	30	33.7
Hypoesthesia to prick	25	28.1
Brushing	13	14.6

Table 3 Associated conditions for neuropathic pain

	Univariate Analysis		Multivariate Analysis	
	OR (95%CI)	*P*-value	OR (95%CI)	*P*-value
Traumatic condition	0.2 (0.1-0.3)	0.01*	…	…
Post surgical condition	2.2 (1.1-4.5)	0.02*	2.3 (1.0-5.5)	0.05
Tendinitis	0.2 (0.1-0.3)	0.001*	…	…
Inflammatory disease	1.4 (0.5-3.1)	0.34	…	…
Myofascial pain	0.3 (0.1-0.6)	0.001*	…	…
Nerve entrapment	17.0 (9.6-29.9)	0.001*	15.6 (8.5-28.6)	0.001*
Degenerative disease	0.5 (0.2-0.9)	0.015*	…	…
Hypertension	0.9 (0.5-1.6)	0.76	…	…
Diabetes mellitus	2.6 (1.4-4.8)	0.002*	…	…
Dyslipidemia	0.3 (0.1-0.7)	0.003*	…	…

CI confidence interval, *OR* odds ratio

* Indicates statistically significant

… Indicates not statistically significant in multivariate analysis

Discussion

The prevalence of neuropathic pain has been reported differently depending on where studies were performed and the associated conditions**.** The prevalence of neuropathic pain in the general population was found to be 6.8-8.2% in European countries[13]. There is little information on the prevalence of neuropathic pain in the Thai orthopaedic department. Neuropathic pain was reported at the Siriraj pain clinic to be 37.8-48.0%[14]. The prevalence of neuropathic pain was reported to be 36% in cancer patients, 10-15% in patients with postherpetic neuralgia, 13-38% in patients with spinal cord injury, 20% in post mastectomy syndrome patients and 16-26% in diabetic patients[15-20]. This study reported 22.3% of patients had neuropathic pain and 16.2% were considered a missed diagnosis of this condition in the orthopaedic out-patient clinic. The patients in this study reported tingling (92.1%), pins and needles (78.7%) and numbness (70.8%) as the most common symptoms of neuropathic pain which can be used by physicians for the early detection of neuropathic pain. Univariate analysis of the associated factors for neuropathic pain was found statistically significant with traumatic conditions, post-surgical, tendinitis disease, muscular-myofascial pain, degenerative conditions, nerve entrapment condition, diabetes mellitus and dyslipidemia. In multivariate analysis, we showed nerve entrapment conditions were the only statistically significant factors associated with neuropathic pain. The sample size was formulated for a prevalence study but 400 participants were sufficient for association analysis. The limitation of this study is that it is cross-sectional in design and therefore cannot establish the causal relationship.

Conclusion

Neuropathic pain is a common condition in orthopaedic out-patient clinics. The present study emphasised on increase awareness of neuropathic

pain in an orthopaedic out-patient clinic. Health care providers should promote the DN4 questionnaire to diagnose neuropathic pain in clinical practice.

Acknowledgements

The authors wish to thank all of the orthopaedic surgeons who took part in this study and BMA hospital for completing the Thai version of DN4 questionnaire.

Potential conflicts of interest

None

References

1. Treede R-D, Jensen TS, Campbell JN, Cruccu G, Dostrovsky JO, Griffin JW, et al. J. Neuropathic pain: Redefinition and a grading system for clinical and research purposes. Neurology 2008; 70; 1630-35.
2. Hansson P. Neuropathic pain: clinical characteristics and diagnostic workup. Eur J Pain 2002; 6: 47-50.
3. Jensen TS, Gottrup H, Sindrup SH, Bach FW. The clinical picture of neuropathic pain. Eur J Pharmacol 2001; 429: 1-11.
4. Galer BS, Dworkin RH. A clinical guide to neuropathic pain. Minneapolis(MN): McGraw-Hill; 2000: 4-6.
5. Dworkin RH. An overview of neuropathic pain: syndromes, symptoms, signs, and several mechanisms. Clin J Pain 2002; 18: 343-9.
6. Dworkin RH, Backonja M, Rowbotham MC, Allen RR, Argoff CR, Bennet GJ, et al. Advances in neuropathic pain: diagnosis, mechanisms, and treatment recommendations. Arch Neurol 2003; 60: 1524-34.
7. Stevens PE, Dibble SL, Miaskowski C. Prevalence characteristics and impact of postmastectomy pain syndrome: an investigation of women's experiences. Pain 1995; 61: 61-8.
8. Jensen MP, Chodroff MJ, Dworkin RH. The impact of neuropathic pain on health-related quality of life: review and implications. Neurology 2007; 68: 1178-82.
9. Meyer-Rosberg K, Kwanstrom A, Kinnman E, Gordh T, Nordfos LO, Kristofferson A. Peripheral neuropathic pain- a multidimensional burden for patients. Eur J Pain 2001; 5: 379-89.
10. Berger A, Dukes EM, Oster G. Clinical characteristics and economic costs of patients with painful neuropathic disorders. J Pain 2004; 5: 143-9.
11. Bouhassir, Attal N, Alchaar H, Boureau F, Bruxelle J, Cunin G, et al. Comparison of pain syndromes associated with nervous or somatic lesion and development of new neuropathic pain diagnostic questionnaire(DN4). Pain 2005; 114: 29-36.
12. Chaudakshetrin P, Prateepavanich P, Chira-Adisai W, Tassanawipas W, Leechavengvongs S, Kitisomprayoonkul W. Cross-cultural adaption to the Thai language of the neuropathic pain diagnostic questionnaire (DN4). J Med Asso Thai 2007; 90: 1860-65.
13. Torrance N, Smith BH, Bennett MI, Lee AJ. The epidemiology of chronic pain of predominantly neuropathic origin. Results from a general population survey. J Pain 2006; 7: 281-9.
14. Chaudakshetrin P. A neuropathic pain survey at Siriraj Pain Clinic. J Med Assoc Thai 2006; 89: 354-61.
15. Grond S, Radbruch L, Meuser T, Sabatowski R, Loich G, Lehmann KA. Assessment and treatment of neuropathic cancer pain following WHO guidelines. Pain 1999; 79: 15-20.
16. Dubinsky RM, Kabbani H, El-Chami Z, Boutwell C, Ali H. Practice parameter: treatment of postherpatic neuralgia: an evidence-based report of the Quality Standards Subcommittee of the American Academy of Neurology. Neurology 2004; 63: 959-65.
17. Werhgen L, Budh CN, Hulting C, Molander C. Neuropathic pain after traumatic spinal cord injury- relations gender, spinal level, completeness, and age at the time of injury. Spinal Cord 2004; 42: 665-73
18. Werhgen L, Hutling C, Molander C. The prevalence of neuropathic pain after non-traumatic spinal cord lesion. Spinal Cord 2007; 45: 609-15.
19. Stevens PE, Dibble SL, Miaskowski C. Prevalence characteristics and impact of postmastectomy pain syndrome: an investigation of women's experiences. Pain 1995; 61: 61-8.
20. Jensen TS, Backonja MM, Hernandez Jimenez S, Tesfaye S, Valensi P, Ziegler D. New perspectives on the management of diabetic peripheral neuropathic pain. Diab Vasc Dis Res 2006; 3: 108-19.

ความชุกและภาวะที่สัมพันธ์กับการปวดเหตุจากพยาธิสภาพประสาทในผู้ป่วยศัลยกรรมกระดูกของโรงพยาบาลกลาง

สมเกียรติ ยงยิ่งศักดิ์ถาวร, พบ, นัชชา กุลสิริอิทธิกร, พยบ

วัตถุประสงค์*: ศึกษาความชุกรวมถึงความสัมพันธ์ของภาวะที่เกี่ยวข้องกับภาวะปวดเหตุจากพยาธิสภาพประสาทในผู้ป่วยที่มารับการรักษาแบบผู้ป่วยนอก แผนกศัลยกรรมกระดูก*

วิธีการศึกษา*: ทำการศึกษาตัดขวาง (cross-sectional) ในผู้ป่วย 400 คนที่เข้ารับการรักษาแบบผู้ป่วยนอก แผนกศัลยกรรมกระดูก โรงพยาบาลกลาง ในเวลาทำการ 9.00-16.00 น วันจันทร์ถึงศุกร์ โดยสุ่มเลือกจากคอมพิวเตอร์พยาบาลประจำแผนกทำการบันทึกข้อมูลพื้นฐาน อาการนำ โรคร่วม และประเมินแบบสอบถาม DN4 ฉบับภาษาไทย (ส่วนสัมภาษณ์) หลังจากนั้นผู้ป่วยเข้ารับการตรวจรักษาตามปรกติและได้รับการประเมินแบบสอบถาม DN4 ฉบับภาษาไทย (ส่วนตรวจร่างกาย) โดยแพทย์ศัลยกรรมกระดูก หลังจากนั้นพยาบาลประจำแผนกรวบรวมข้อมูลทั้งหมดและวินิจฉัยการปวดเหตุจากพยาธิสภาพประสาทเมื่อคะแนนจากแบบสอบถาม DN4 ฉบับภาษาไทย มากกว่าหรือเท่ากับ 4 โดยแบบสอบถาม DN4 ฉบับภาษาไทยมีการทดสอบความถูกต้องในการแปลเป็นภาษาไทยแล้ว คำนวณค่าสถิติพื้นฐาน ใช้สถิติไคสแควร์ เพื่อคำนวณการเปรียบเทียบ และใช้โลจิสติก รีเกรทชั่น สำหรับการวิเคราะห์หลายตัวแปร

ผลการศึกษา*: อัตราความชุกของการปวดเหตุจากพยาธิสภาพประสาท ในผู้ป่วยที่มารับการรักษาแบบผู้ป่วยนอก แผนกศัลยกรรมกระดูก พบร้อยละ 22.3 พบอัตราการวินิจฉัยผิดพลาด ร้อยละ 16.2 ผู้ป่วยที่มีเส้นประสาทถูกกดทับ มีความสัมพันธ์กับการปวดเหตุจากพยาธิสภาพประสาทมีความสัมพันธ์กันอย่างมีนัยสำคัญทางสถิติ อาการชาเหมือนเป็นเหน็บ (ร้อยละ 92.1), อาการเจ็บชาคล้ายเข็มตำ (ร้อยละ 78.7), ชาไร้ความรู้สึก (ร้อยละ 70.8) เป็นอาการที่พบได้บ่อยที่สุดและเหมาะสำหรับใช้สังเกตในการตรวจทางคลินิก*

สรุป*: การปวดเหตุจากพยาธิสภาพประสาท ในผู้ป่วยที่มารับการรักษาแบบผู้ป่วยนอก แผนกศัลยกรรมกระดูก พบได้บ่อยและมีการวินิจฉัยพลาดได้ การศึกษาบ่งชี้ว่าควรมีความตระหนักถึงภาวะดังกล่าวมากขึ้น และควรสนับสนุนให้ใช้แบบสอบถาม DN4 เพื่อการวินิจฉัยการปวดเหตุพยาธิสภาพประสาทในแผนกผู้ป่วยนอก*

Effect of Surgeon Handedness on Coronal Alignment in Total Knee Arthroplasty

Opas Chaiyamahapruek, MD

Department of Orthopaedic Surgery, Samutsakhon Hospital, Samutsakhon, Thailand

Purpose: *To study the effect of surgeon handedness by comparing coronal alignment in total knee arthroplasty (TKA) between left and right sides.*
Methods: *This study retrospectively reviewed the medical records and knee radiographs of patients who underwent total knee arthroplasty using conventional techniques from 2010 to 2012. There were 49 right knees and 47 left knees in 78 patients. The knee radiographs taken before and after surgery were used to measure the tibiofemoral angle and the coronal alignment of the femoral and tibial components. A value within the optimum ±3º was defined as "acceptable" and a value over the optimum ±3º was defined as an "outlier".*
Results: *The postoperative tibiofemoral angle showed outliers in 7 right TKAs and 11 left TKAs. The coronal alignment of the femoral component showed outliers in 9 right TKAs and 7 left TKAs. The coronal alignment of the tibial component showed outliers in 2 right TKAs and 10 left TKAs. There was a significant difference in the outliers of coronal alignment of the tibial component between right and left TKAs.*
Conclusion: *Surgeon handedness affects the coronal alignment of the tibial component. There were more outliers of the coronal alignment of the tibial component in left knees when performed by right-handed surgeons.*

Keywords: *Surgeon handedness, coronal knee alignment, total knee arthroplasty*

The Thai Journal of Orthopaedic Surgery: 37 No.2-4: 49-54
Full text. e journal: *http://www.rcost.or.th, http://thailand.digitaljournals.org/index.php/JRCOST*

Introduction

Currently, total knee arthroplasty (TKA) is a common procedure which is increasingly performed in Thailand. The survival and functional outcomes of TKAs are related to the alignment[1,2]. Malalignment may cause pain, a limited range of motion, joint instability, wear of the polyethylene liner and prosthesis loosening[1,3-5]. Numerous general surgical literatures had documented the effect of handedness on operative psychomotor performance[6-8]. In orthopaedic surgery, handedness and laterality play a larger role but few orthopaedic literatures mention handedness and laterality as a major factor affecting outcomes. In 2007, Mehta and Lotke[9] reported that right TKAs had a better functional outcome at the 1 year follow up than left TKAs performed by a right-handed surgeon.

However, there has been no report showing the effect of surgeon handedness on the coronal alignment of TKAs. Therefore, the purpose of this study was to evaluate the effect of surgeon handedness by comparing coronal alignment between right TKAs and left TKAs. We hypothesized that right TKAs had a more optimal coronal alignment than left TKAs when performed by right-handed surgeons.

Correspondence to: Chaiyamahapruek O, Department of Orthopaedic Surgery, Samutsakhon Hospital, Samutsakhon 74000, Thailand
E-mail: opaspmk@yahoo.com

Patients and methods

The medical records and the knee radiographs of every patient treated with total knee arthroplasty from January 2010 to December 2012 in Samutsakhon Hospital were reviewed. All operations were performed by the same right-handed surgeon team. Conventional intramedullary femoral and extramedullary tibial guiding systems were used in all cases. Exclusion criteria were revision total knee arthroplasty, unicondylar arthroplasty, extra-articular deformity and loss of the medical records or the radiographs. The parameters used included gender, age, body mass index, operative time, complication, pre- and postoperative tibiofemoral angle and the coronal alignment of the femoral and tibial components. All patient data were categorized based on the side of procedure. This study was approved by the ethical committee of Samutsakhon Hospital.

Surgical technique

The surgeon performed the procedure standing on the side of the knee to be operated on. The patient was in a supine position. The operation was carried out through a midline incision via a medial parapatella approach. The patients who underwent total knee arthroplasty used cemented mobile-bearings, PS design (e.motion® PS, B Braun, Aesculap, Tuttlingen, Germany) under gap technique and cemented fixed bearings, PS design (Nexgen LPS, Zimmer, Warsaw, United States) under measure resection technique. Conventional

intramedullary femoral and extramedullary tibial guiding systems were used in all cases. The posterior cruciate ligament was sacrificed in all cases. The femoral component was aligned to 6° of valgus using an intramedullary guide inserted just medial to the trochlea groove, approximately 1 cm anterior to the femoral insertion of the posterior cruciate ligament. A proximal tibial cut was set perpendicular to the mechanical axis of the tibia. All patellae were not resurfaced. All implants were fixed with a cemented technique. Operations were performed by 3 general orthopaedic surgeons. They had, on average, 5 years' experience in TKA.

Radiological measurements

The pre- and postoperative standardized weight-bearing anteroposterior knee radiographs were reviewed and the angles were manually measured by a goniometer. The weight-bearing anteroposterior knee radiograph used an 11×14 inch film with the knee in full extention. The tube-to-film distance was 100 cm with usual exposure setting of 50 kV and 3.2 mA. All radiographs were obtained with the same technique and standard position. Before measurements were taken, all radiographs were blinded for patient identity and side, and then were evaluated by three individuals who did not know about the details of this study. The mean of each parameter were recorded and used for evaluation in the study.

The tibiofemoral angle was formed by the intersection of the line of the proximal shaft of the tibia and a line through the femoral midcondylar point and the center of the distal femoral shaft.

The coronal alignment of the femoral component was measured as the angle between the femoral shaft and transcondylar line of the femoral component.

The coronal alignment of the tibial component was measured as the angle between the mechanical axis of the tibia and the tibial base plate (Fig. 1).

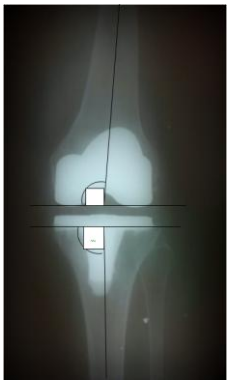


Fig. 1 Measurement of component alignment in the coronal plane; α, the coronal alignment of the femoral component; β, the coronal alignment of the tibial component

A value of parameters within the optimum ±3º was defined as "acceptable" and a value over the optimum ±3º was defined as an "outlier".

Statistical analysis

Analysis of the data was performed using the statistical package for social sciences (SPSS) software, version 11.5 (SPSS Inc., Chicago, Illinois). The continuous variables between the two groups were compared using an independent sample *t*-test. The categorical variables between the two groups were compared using Pearson Chi-square and Fisher's exact test. Statistical significance was considered when the *P*-value was < 0.05. The inter-observer reliability was analyzed using level of agreement and a 95% limit of agreement (Bland and Altman, 1986).

The sample size calculation was based on an alpha error of 0.05, a beta error of 0.2, the probability to have outlier in right TKAs was 5% and the expected outlier in left TKAs was 25%. The overall sample size was 38 patients per group ($N = [2(Z_\alpha+Z_\beta)^2 P(1-P)]/(P_1-P_2)^2$).

Results

There were 31 right TKAs and 29 left TKAs and 18 bilateral TKAs of 78 patients with a mean age of 63.1 years (ranging from 50-77 years). The age, number of cases, body mass index, operative time, preoperative tibiofemoral angle and the prosthesis design of the two groups were not statistically significant. Cemented mobile-bearings, PS design (e.motion® PS, B Braun, Aesculap, Tuttlingen, Germany) were used in 23 right TKAs and 22 left TKAs. Cemented fixed bearings, PS design (Nexgen LPS, Zimmer, Warsaw, United states) were used in 26 right TKAs and 25 left TKAs (Table 1).

The postoperative tibiofemoral angle, coronal alignment of femoral component and coronal alignment of tibial component were not statistically different (Table 2).

As shown in table 3, the postoperative tibiofemoral angle (optimum=186°) showed 7 outliers (14.3%) in right TKAs and 11 outliers (23.4%) in the left TKAs group (*P*=0.25). The coronal alignment of the femoral component (optimum=96°) showed 9 outliers (18.4%) in right TKAs and 7 outliers (14.9%) in left TKAs (*P*=0.65). The coronal alignment of the tibial component (optimum=90°) showed 2 outliers (4.1%) in right TKAs and 10 outliers (21.3%) in left TKAs (*P*=0.01). The complication rate was not significantly different between groups (*P*=0.11). There were 2 cases (4.3%) of patella tendon tear and 1 case (2.1%) of periprosthetic fracture of the tibia in the left TKAs.

Table 1 Demographic data of TKA patients

	Right	**Left**	***P*-value** [c]
Age (years)	63.2 ± 7. 1	63.0 ± 6.9	0.85
No. of cases (male/female)	9/40	3/44	0.12 [b]
Body mass index	26.8 ± 4.3	25.5 ± 5.0	0.16
Operative time (minutes)	108.9 ± 20.9	108.1 ± 25.0	0.87
Preoperative tibiofemoral angle	173.2 ± 6.7	173.7 ± 7.2	0.74
Prosthesis design (e.motion®PS/Nexgen LPS)	23/26	22/25	0.99 [a]

[a] χ^2 test (Pearson Chi-square) comparing between the categorical variables of the two groups

[b] χ^2 test (Fisher's exact test) comparing between the categorical variables of the two groups when data in cell have an expected count of less than 5

[c] Independent sample *t*- test comparing the two groups

Table 2 Coronal alignment angulation between right TKAs and left TKAs

	Right	**Left**	***P*-value** [c]
Postoperative tibiofemoral angle	185.5 ± 2.3	185.2 ± 3.1	0.59
Coronal alignment of femoral component	95.0 ± 2.2	94.8 ± 2.0	0.62
Coronal alignment of tibial component	90.4 ± 1.5	90.4 ± 2.8	0.92

[c] Independent sample *t*- test comparing the two groups

Table 3 Coronal alignment outlier between right TKAs and left TKAs

	Right	**Left**	***P*-value**
Postoperative tibiofemoral angle	7 (14.3%)	11(23.4%)	0.25 [a]
Coronal alignment of the femoral component	9 (18.4%)	7(14.9%)	0.65 [a]
Coronal alignment of the tibial component	2 (4.1%)	10(21.3%)	0.01 [b]

[a] χ^2test (Pearson Chi-square) comparing between the categorical variables of the two groups

[b] χ^2 test (Fisher's exact test) comparing between the categorical variables of the two groups when data in cell have an expected count of less than 5

Table 4 Reliability and agreement of coronal alignment angulation.

Variables	Intraclass correlation coefficient	Standard error	Difference		95% Limits of agreement
			Average	Standard deviation	
Preoperative tibiofemoral angle					
- Observer A vs B	0.97	0.01	-0.81	1.49	-3.73, 2.11
- Observer A vs C	0.95	0.01	-1.28	2.01	-5.22, 2.66
Postoperative tibiofemoral angle					
- Observer A vs B	0.84	0.03	-1.35	1.33	-3.96, 1.25
- Observer A vs C	0.41	0.05	-3.33	2.33	-7.89, 1.23
Coronal alignment of the femoral component					
- Observer A vs B	0.88	0.02	-0.51	0.99	-2.45, 1.44
- Observer A vs C	0.56	0.056	-1.65	1.75	-5.07, 1.77
Coronal alignment of the tibial component					
- Observer A vs B	0.84	0.03	-0.82	1.01	-2.81, 1.16
- Observer A vs C	0.61	0.05	-1.67	1.58	-4.77, 1.43

The results of the inter-observer reliability of measurement using level of agreement and a 95% limit of agreement were moderate to high reliability and agreement (Table 4).

Discussion

The surgical performance and outcomes had been affected by three factors (kinematic restriction, reduced tactile feedback and increased perceptual processing consequent on operating from a direct image of the operating field)[6]. Mehta and colleagues[9] offer the laterality of the operative site with respect to the surgeon handedness as a fourth factor. Handedness is a tendency to use one hand rather than the other and laterality is the preference of using one side of the body over the other. There were numerous studies in general surgery documenting the effect of handedness as an independent factor affecting surgical techniques and outcomes[6-8]. Adusumilli et al.[10] examined left-handed surgeons and reported that 3% of left-handed surgeons had received specific mentoring, 10% of medical schools have laterality training programs and 13% provide left handed instruments. Handedness and laterality not only affected left-handed surgeons but also right-handed surgeons. Surgeons may prefer to perform an operation on one side over the other because they feel more comfortable and it is easier to perform the operation.

There are few reports in orthopaedic surgery that mentioned handedness and laterality although they played a significant role. Maloney et al.[11] reported that left side sliding hip screws in the fractured neck of the femur had more technical failures than right side sliding hip screws when performed by right handed surgeons. Mehta and Lotke[9] reported that right TKAs had better functional outcomes at a 1 year follow up than left TKAs performed by a right-handed surgeon standing on the side of the operative procedure.

The results of this study showed that the surgeon handedness affects the coronal alignment of TKAs. The left TKAs had significantly more outliers of coronal alignment of the tibial component than right TKAs when performed by right-handed surgeons standing on the side of the operative procedure. The reason for these differences may be due to misvisual perception during setting the extramedullary tibial guide and inaccurate bone resection due to using the non-dominant hand to perform the tibial cut. Lui and colleagues[12] found that right-handed orthopaedic surgeons do not tend to reposition themselves to utilize their dominant hand when performing an operation but instead use their non-dominant hand. For example, when performing a left TKA, a right-handed surgeon tended to use the left hand to perform the tibial cut. The outliers of coronal alignment of the femoral component were not statistically different but it was more than the outliers of coronal alignment of the tibial component (16.7% vs 12.5%). The outliers of coronal alignment of the right femoral component may be caused by inaccurate bone resection due to during the procedure the surgeons had changed position with the assistants and used their non-dominant hand to perform the distal femoral cut. However, the outliers of coronal alignment of the left femoral component may be caused by visual misjudgment of the entry point of the intramedullary femoral guiding system. Visual misjudgment of the entry point may have less effect on alignment than using a non-dominant hand to perform the bone cut.

The outliers of coronal alignment of TKAs arise not only from the alignment system, but also from factors related to the surgeons and patients. The handedness and laterality including surgical experience may produce malalignment. In previous studies, postoperative alignment of the limb exceeded a range of ±3º in up to 30% of cases[13-15]. In this study, the overall outliers of the postoperative tibiofemoral angle were 18.8%. These findings agree with those of Petersen and Engh[13] and Mahaluxmivala et al.[15] that showed 26% and 25% outliers of postoperative tibiofemoral angle, respectively. In a recent meta-analysis of 29 studies comparing computer navigation to conventional instrument TKA, 31.8% of conventional TKA had more than 3° of varus and valgus alignment[16]. The overall outliers of coronal alignment of the femoral component were 16.7% and the overall outliers of coronal alignment of the tibial component were 12.5%. Similar results were reported by Kim et al.[17] in 520 TKAs. They found 10% of outliers of coronal alignment of the femoral component and 15% of outliers of coronal alignment of the tibial component. Although the surgeons in this study had, on average, 5 years' experience in TKA, there is no difference in the results of overall coronal alignment outliers of TKA between this study and previous studies from specialist centers[13,14,17].

In the present data, all complications were found in the left TKAs including patella tendon tear and periprosthetic fracture. These complications may be caused by some difficulties in the approach of left TKAs by the right-handed surgeon standing on the left side.

Long-leg weight-bearing radiographs have been the gold standard for assessing overall limb alignment but they are not routinely used due to the added cost and difficult techniques. A previous study had shown the correlation between anatomical and mechanical axes. There is no significant difference between measurements from standard knee and hip to ankle radiographs[13]. Although the inter-observer reliability of measurement in this study was moderate to high reliability and agreement, there may be some errors

of measurement caused by misidentification of the landmarks or misinterpretation of the goniometer. These errors can be reduced by using modern digital radiographs and measuring by computerized analysis tools.

To avoid the potential problems when operating on the non-dominant side, orthopaedic surgeons should have non-dominant hand training, familiarity with surgical technique and prosthesis, adjust one's body position during surgery and special precautions when handling soft tissue or making a bone cut[9]. Now computer assisted surgery has a significant role in orthopaedic surgery. It may decrease technical errors that come from the effects of handedness and laterality

This study has some limitations. It is a retrospective study, with a small sample size, and lack of clinical data to correlate with handedness. Further study designs evaluating the effect of surgeon handedness should use large sample sizes including outcomes from left-handed surgeons and a prospective study with clinical results.

Conclusion

There were more outlying results of the coronal alignment of the tibial component of left TKAs when performed by right-handed surgeons. Surgeon handedness does have an effect on coronal alignment of TKAs. Surgeons should concern about the effect of handedness and laterality to prevent unexpected results when performing on their non-dominant side. The results from this study could be useful for preventing coronal malalignment in TKAs which are related to the survival outcome and functional outcome.

Acknowledgements

The author would like to thank Phusapong Srisawat, MD, Department of Orthopaedics, Phramongkutklao Hospital, for kindly reviewing this manuscript.

Potential conflict of interest

None

References

1. Rand JA, Coventry MB. Ten-year evaluation of geometric total knee arthroplasty. Clin Orthop Relat Res 1988; 232: 168-73.
2. Ranawat CS, Boachie-Adjei O. Survivorship analysis and results of total condylar knee arthroplasty. Eight-to 11-year follow-up period. Clin Orthop Relat Res 1988; 226: 6-13.
3. Bargren JH, Blaha JD, Freeman MA. Alignment in total knee arthroplasty. Correlated biomechanical and clinical observations. Clin Orthop Relat Res 1983; 173: 178-83.
4. Ritter MA, Faris PM, Keating EM, Meding JB.Postoperative alignment of total knee replacement. Its effect on survival. Clin Orthop Relat Res 1994; 299: 153-6.
5. Wasielewski RC, Galante JO, Leighty RM, Natarajan RN, Rosenberg AG. Wear patterns on retrieverd polyethylene tibial inserts and their relationship to technical considerations during total knee arthroplasty. Clin Orthop Relat Res 1994; 299: 31-43.
6. Hanna GB, Drew T, Clinch P, Shimi S, Dunkley P, Hau C, Cuschieri A. Psychomotor skills for endoscopic manipulations: differing abilities between right and left handed individuals. Ann Surg. 1997; 225: 333-8.
7. Pouw L, Tulloh B. Laparoscopic cholecystectomy for the left-handed surgeon. Br J Surg. 1995; 82: 138.
8. Schueneman AL, Pickleman J, Freeark RJ. Age, gender, lateral dominance, and prediction of operative skill among general surgery residents. Surgery 1985; 98: 506-15.
9. Mehta S, Lotke PA. lmpact of surgeon handedness and laterality on outcomes of total knee arthroplasties: should right-handed surgeons do only right TKAs ? Am J Orthop 2007; 36: 530-3.
10. Adusumilli PS, Kell C, Chang JH, Tuorto S, Leitman IM. Left-handed surgeons: are they left out? Curr Surg 2004; 61: 587-91.
11. Moloney D, Bishay M, Ivory J, Pozo J. Failure of the sliding hip screw in the treatment of femoral neck fractures: 'left-handed surgeons for left-sided hips'. Injury 1994; 25 Suppl 2: S9-13.
12. Lui DF, Baker JF, Nfilfa G, Perera A, Stephens M. Hand dominance in orthopedic surgeons. Acta Orthop Belg 2012; 78: 531-7.
13. Petersen TL, Engh GA. Radiographic assessment of knee alignment after total knee arthroplasty. J Arthroplasty 1988; 3: 67-72.
14. Mielke RK, Clemens U, Jens Jh, Kershally S. Navigation in knee endoprosthesis implantation: pleliminary experiences and prospective comparative study with conventional implantation technique. Z Orthop Ihre Grenzgeb 2001; 139: 109-16.
15. Mahaluxmivala J, Bankes MJ, Nicholai P, Aldam CJH, Allen PW. The effect of surgeon experience on component positioning in 673 press fit condylar cruciate-sacrificing total knee arthroplasties. J Arthroplasty 2001; 16: 635-40.
16. Mason JB, Fehring TK, Estok R, Banel D, Fahrbach K. Meta-analysis of alignment outcomes in computer-assisted total knee arthroplasty surgery. J Arthroplasty 2007; 22: 1097-106.
17. Kim YH, Park JW, Kim JS. Computer-navigated versus conventional total knee arthroplasty: a prospective randomized trial. J Bone Joint Surg (Am) 2012; 94: 2017-24.

ผลของมือข้างถนัดของศัลยแพทย์ต่อแนวแบ่งหน้าหลังในการผ่าตัดเปลี่ยนใส่ข้อเข่าเทียม

โอภาส ไชยมหาพฤกษ์, พบ

วัตถุประสงค์: *เพื่อศึกษาผลของมือข้างถนัดของศัลยแพทย์ต่อแนวแบ่งหน้าหลัง (coronal) โดยเปรียบเทียบระหว่างการผ่าตัดเปลี่ยนใส่ข้อเข่าเทียมข้างขวากับข้างซ้าย*

วิธีการศึกษา: *ทำการศึกษาย้อนหลังจากเวชระเบียนและภาพถ่ายรังสีของผู้ป่วยที่ทำการผ่าตัดเปลี่ยนใส่ข้อเข่าเทียมตั้งแต่มกราคม พ.ศ.2553 ถึง ธันวาคม พ.ศ.2555 ในผู้ป่วยจำนวน 78 ราย เป็นข้อเข่าขวา 49 ราย ข้อเข่าซ้าย 47 ราย ภาพถ่ายรังสีก่อนและหลังการผ่าตัดได้ถูกนำมาวัดมุม tibiofemoral, coronal alignment of femoral component และ coronal alignment of tibial component ค่ามุมที่เหมาะสม ± 3º ให้นิยามว่า รับได้ (acceptable) ส่วนค่ามุมที่เหมาะสมมากกว่า ±3º ให้นิยามว่า นอกแนว (outlier) นำค่าที่วัดได้มาเปรียบเทียบระหว่างข้อเข่าเทียมข้างขวากับข้างซ้าย*

ผลการศึกษา: *พบนอกแนว (outlier) ของมุม tibiofemoral ภายหลังการผ่าตัดเปลี่ยนใส่ข้อเข่าเทียมข้างขวา 7 ราย ข้อเข่าเทียมข้างซ้าย 11 ราย นอกแนว (outlier) ของ coronal alignment of femoral component ในข้อเข่าเทียมข้างขวา 9 ราย ข้อเข่าเทียมข้างซ้าย 7 ราย นอกแนว (outlier) ของ coronal alignment of tibial component ในข้อเข่าเทียมข้างขวา 2 ราย ข้อเข่าเทียมข้างซ้าย 10 ราย พบว่ามีความแตกต่างอย่างมีนัยสำคัญทางสถิติของนอกแนว (outlier) ของ coronal alignment of tibial component ระหว่างข้อเข่าเทียมข้างขวากับข้อเข่าเทียมข้างซ้าย*

สรุป: *มือข้างถนัดของศัลยแพทย์ มีผลกระทบต่อแนวในระนาบ coronal ของข้อเข่าเทียม โดยพบว่ามีนอกแนว (outlier) ของ coronal alignment of tibial component ในข้อเข่าเทียมข้างซ้ายมากกว่าข้อเข่าเทียมข้างขวาอย่างมีนัยสำคัญทางสถิติในการผ่าตัดโดยศัลยแพทย์ถนัดมือขวา*

Adipokines: Metabolic link between knee osteoarthritis and obesity

Thitiya Poonpet, PhD, Sittisak Honsawek, MD

Department of Biochemistry, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand

Osteoarthritis (OA) is a heterogeneous and multifactorial process of chronic degenerative joint disorder that involves not only articular cartilage, but also synovium, subchondral bone, and surrounding muscles and ligaments. Obesity is a well known risk factor of the incidence and prevalence of osteoarthritis and is believed to play a deleterious part in knee OA by the increment in mechanical stresses on the joints. The role of obesity in knee OA is much more complicated than previously thought. Adipokines, cytokines mainly produced by adipose tissue, may play a potential role in knee OA. In this review, we summarize the recent advances in adipokine research in knee osteoarthritis, focusing on leptin, adiponectin, visfatin, and resistin, and also the essential role of newly identified adipokines such as chemerin, lipocalin, and omentin.

Keywords: *Adipokines, knee osteoarthritis, obesity*

The Thai Journal of Orthopaedic Surgery: 37 No.2-4: 55-65
Full text. e journal: *http://www.rcost.or.th, http://thailand.digitaljournals.org/index.php/JRCOST*

Introduction

Osteoarthritis (OA) is a highly prevalent degenerative joint disease estimated to affect more than 37% of people who are over 60 years of age[1]. The disease is characterized by fibrillation of articular cartilage, alterations in subchondral bone, the formation of osteophytes, and low-level synovial inflammation. Its etiology is largely complicated since both genetic factors and non-genetic factors such as age, gender, joint injury and obesity are considered as important risk factors[2]. Knee OA is among the most common burden diseases in developed countries, and its prevalence is set to continue to increase in the near future, likely due to aging of the population[3].

Obesity and osteoarthritis

Obesity has long been considered as an important risk factor for the development and progression of OA. The association between OA and obesity is strongest in the knee; the joint that supports almost the whole weight of our body[4, 5]. A study in the British population revealed that women in the highest body mass index (BMI) tertile had a higher risk of knee OA (6 times) and bilateral knee OA (18 times), compared with women in the lowest BMI tertile[6]. The same trend of results was also obtained from a study in African-American and Caucasian women[7]. In addition, a longitudinal study of both genders indicated a 40% increased risk for developing knee OA[8]. It is generally accepted that obesity may lead to cartilage destruction by increasing the mechanical stress of the joints or alterations of cartilage matrix components. However, quite new advances in the knowledge of white adipose tissue (WAT) suggested that besides from biomechanical effects, metabolic effects are also involved in OA[9]. Moreover, several studies demonstrated that fat excess is also associated with OA in non-weight-bearing joints, such as those of the hand. For example, there was a study which reported a two-fold increase in the risk of hand OA in obese patients[10], suggesting that metabolic factors released mainly by adipose tissue may be responsible for the high prevalence of OA among overweight individuals[11].

Knee osteoarthritis as an inflammatory disease

Although knee OA was described as a 'wear-and-tear' noninflammatory disease, it is now recognized that metabolic and inflammatory environments contribute to the symptoms and progression of knee OA[12, 13]. Findings in the 1990s indicated that cartilage, bone, the synovium and infrapatellar fat pads are sources of inflammatory mediators involved in the pathophysiological changes in OA[14]. Many mediators with inflammatory properties, such as prostaglandins and cytokines can increase matrix metalloproteinases (MMPs) production by chondrocytes and synovial cells, which finally increases cartilage degradation. Therefore, OA has also been mentioned as being part of a metabolic syndrome[15].

Correspondence to: Honsawek S, Department of Biochemistry and Orthopaedics, Faculty of Medicine, Chulalongkorn University and King Chulalongkorn Memorial Hospital, Thai Red Cross Society, Rama IV road, Patumwan, Bangkok, 10330, Thailand
E-mail: sittisak.h@chula.ac.th

Obesity and adipokines

Obesity is currently classified with a chronic low-grade inflammatory status. The metabolic link between obesity and OA could be the adipocytokines (or adipokines) produced by adipose tissue. White adipose tissue (WAT) is considered mainly to be an energy storage portal. However, it is now recognized as a metabolically active endocrine organ with the capacity to secrete proinflammatory agents including classical cytokines [e.g., interleukin-6 (IL-6), interleukin-1β (IL-1β) and tumour necrosis factor-α (TNF-α)], as well as adipokines, such as leptin, adiponectin, resistin and visfatin[16-18]. Adipokines are hormone and cytokine like substances which play a critical role in several pathways including not only glucose and lipid metabolism but also immune and inflammatory responses[19]. Over the past decade, adipokines have prompted much interest in OA pathophysiological research based on the fact that they play an important role in cartilage and bone homeostasis. The involvement of adipokines in OA can be direct joint degradation or the control of local inflammation. Four main adipokines (leptin, adiponectin, resistin, and visfatin) levels have been locally detected in the synovial fluid of knee OA joints. Adipokines are produced in knee OA joints by chondrocytes, osteoblasts, osteoclasts, as well as infrapatellar fat pads. It was suggested that local (synovial fluid) and systemic (serum) adipokine levels would be associated with cartilage degradation and synovial inflammation[20]. Therefore, the aim of this review is to include the current reports regarding the association between knee osteoarthritis and potential adipokines including leptin, adiponectin, resistin, and visfatin, of which their involvements in osteoarthritis are summarized in Table 1.

Table 1 Involvements of four main adipokines in osteoarthritis

Important issues	Leptin	Adiponectin	Visfatin	Resistin
Association with BMI	positive	negative	positive	not clear
Plasma levels between genders	women > men	women > men	women > men	women > men
Plasma levels between groups	OA > control	control > OA	OA > control	OA > control
Levels in OA patients	SF > plasma	plasma > SF	SF > plasma	plasma > SF
Roles in cartilage homeostasis	- ↑ proteases - ↑ inflammatory cytokines - ↓ growth factor - ↓chondrocytes proliferation	- ↑ proteases - ↑ inflammatory cytokines - ↓ MMP-13 - ↑ TIMP-2	- ↑ proteases - ↑ inflammatory cytokines - ↑ proteoglycan degradation - ↓ proteoglycan production	- ↑ proteoglycan degradation - ↓ proteoglycan production
Roles in bone formation	- expressed in osteoblasts and osteophyte - increase bone growth	- expressed in osteoblasts and osteophyte	- expressed in osteoblasts, osteoclasts and osteophyte	- expressed in osteoblasts, osteoclasts and osteophyte
Associated biomarkers	- bone formation - joint metabolism	- cartilage degradation - collagen degradation	- inflammation - collagen degradation - aggrecan degradation	- joint metabolism
Associated clinical data	- prevalence - progression - grade of cartilage degeneration	- Ahlback score -Lequesne Index - severity (negatively)	KL-score	prevalence

BMI, Body mass index, *KL*, Kellgren-Lawrence, *OA*, Osteoarthritis, *SF*, Synovial fluid

Leptin

Leptin is a 16 kDa nonglcosylated adipokine encoded by the *ob* (obese) gene[21]. The best known effects of leptin are its involvement in body weight homeostasis, since it decreases food intake but increases energy expenditure at the hypothalamic level[22]. It is synthesized exclusively by adipocytes, and its circulating levels are correlated with the amount of body fat[23]. Obese individuals generally produce higher amounts of leptin. This adipokine exerts its biological activities through the activation of its specific receptors (Ob-

R) which belong to the class I cytokine receptor superfamily. In humans, at least five isoforms of leptin receptor, resulting from alternative splicing of the *db* (diabetes) gene exist[24]. However, only the long isoform (Ob-Rb) seems to be functional. The Ob-Rb contains the intracytoplasmic motifs required for the activation of the JAK-STAT system[25]. Mutations in either the *ob* gene or *db* gene results in an obese phenotype in mice[26]. Currently, it is increasingly evident that leptin plays a significant role in the OA pathophysiology by modulating the bone and cartilage metabolism. Moreover, ob/ob leptin-deficient mice develop resistance to antigen-induced arthritis[27].

Leptin and its receptor can be secreted by chondrocytes, osteophytes[28] and the synovium, as well as infrapatellar fat pads[29]. Plasma leptin concentration was significantly correlated with BMI, in both OA patients and normal controls[30], suggesting its role as a metabolic link between OA and obesity. It has been reported that a 1 ng/ml higher plasma leptin concentration was associated with 7% higher odds ratio of having knee OA, after adjustments for age, ethnicity and BMI[31]. Nevertheless, leptin levels in synovial fluid were 3 to 11 times higher than those in paired plasma samples[29]. This difference was more obvious in women than in men. Therefore, locally produced leptin may play more significant roles in bone metabolism regulation than circulating leptin.

Leptin shows catabolic effects in OA cartilage by increasing metalloproteinases (MMPs) enzymes such as MMP-1, MMP-3, MMP-9 and MMP-13, as well as cysteine proteases production at both the gene and protein levels[32, 33]. In addition, the gene expression of *ADAMTS-4* and -5, which are responsible for the degradation of aggrecan, were considerably increased after treatment with leptin. Moreover, Bao et al. have demonstrated that leptin downregulated the anabolic factors such as basic fibroblast growth factors (bFGF) in mouse articular cartilage. These results suggest a prominent catabolic effect of leptin as a proinflammatory factor on cartilage metabolism in knee OA[34].

Nitric oxide (NO) is a well-known proinflammatory mediator which promotes chondrocyte phenotype loss, apoptosis, as well as MMPs activation. The production of type 2 nitric oxide synthase (NOS2) in cultured human and murine chondrocytes is activated by the combination of leptin and interferon-γ[35]. Recently, leptin has also been reported to enhance cyclooxygenase-2, prostaglandin E2, IL-6, and IL-8 production in human chondrocytes[36]. Interestingly, leptin also had a negative effect on chondrocyte proliferation since it reduced OA chondrocytes proliferation for the short term-treatment (48 hours) and reduced both normal and OA chondrocytes proliferation for the long-term treatment (7 days)[37].

Leptin is also involved in osteoblast dysfunction in OA. It has recently been found that leptin acts as a bone growth regulator by inducing collagen synthesis, osteoblast proliferation, bone mineralization, and also endochondral ossification[38-40]. The increased production of leptin in OA subchondral osteoblasts is associated with the increased levels of alkaline phosphatase, osteocalcin, collagen type I, and TGF-β1 (transforming growth factor-β1)[41]. Moreover, the findings of immunohistochemical studies showed high leptin expression in osteophytes[11]. Berry et al.[42] have revealed that the level of serum leptin was significantly associated with the level of bone formation markers, such as osteocalcin and procollagen type I N-terminal propeptide (PINP). In addition, leptin was positively associated with the cartilage biomarkers such as urine C-terminal telopeptide of type II collagen (uCTX-II), serum cartilage oligomeric matrix protein (sCOMP), and serum procollagen type IIA N-terminal propeptide (sPIIANP), serum hyaluronic acid (sHA) and serum N-terminal propeptide of type III procollagen (sPIIINP) after adjustment for gender and age. In contrast, baseline expression levels of soluble leptin receptors OB-Rb were negatively associated with 2-year changes of the cartilage formation biomarkers PIIANP and osteocalcin levels, but positively associated with cartilage defects scores and cartilage volume loss, independent of age, gender, and BMI[42].

In a 5-year cohort study, plasma leptin levels seemed to be positively associated with the occurrence of radiographic knee OA. Moreover, it showed a positive association with knee OA progression in subjects who have radiographic knee OA baseline. However, the association disappeared after adjustment for BMI[42]. Leptin expression has been reported to be associated with the grade of cartilage degeneration. In advanced grade OA cartilage, leptin and its receptor (Ob-Rb) levels were significantly increased compared to healthy or adjacent mildly affected cartilage[37]. On the contrary, Berry et al. did not find any association between plasma leptin levels and knee OA with grade 4 Kellgren-Lawrence (KL)-score and found no association between baseline plasma leptin levels, 2-year alterations of cartilage volume, and defects in knee OA patients[42].

Adiponectin

Adiponectin is a 244-residue protein that is synthesized mainly by WAT. Its main metabolic properties are that it increases insulin sensitivity, improves glucose metabolism, increases fatty acid oxidation, and antiatherogenesis[22, 43, 44]. In plasma, it is present in three molecular forms: trimers (low

molecular weight complexes), hexamers (mid-molecular weight complexes), and 12- to 18-hexamers (high molecular weight, HMW, complexes)[45]. Adiponectin acts via two receptors, AdipoR1 and AdipoR2. AdipoR1 is found in skeletal muscle, cartilage, bone and the synovium, whereas AdipoR2 is found predominantly in the liver[46, 47]. The adiponectin knockout mice develop severe insulin resistance and exhibit lipid accumulation in muscles when placed on a high fat/sucrose diet[48].

In general, adiponectin is detectable in both plasma and synovial fluid but shows different patterns of distribution[29]. In the blood, it circulates in high concentrations (0.01% of total serum protein) exceeding those in the matched synovial fluid[28]. Serum adiponectin levels are inversely correlated with BMI, lower in obese individuals and elevate with weight loss[48,49]. Women have remarked higher plasma adiponectin levels than men[50], whereas the effect of age on circulating adiponectin levels are inconsistent. In OA patients, serum adiponectin levels were reported to be lower than in healthy controls[51]. In addition, the levels of adiponectin in OA plasma were almost 100-fold higher than in OA synovial fluid, and these plasma and synovial fluid levels showed an inverse correlation[47]. Recently, Distel et al. have shown increased adiponectin levels in the infrapatellar fat pads in knee OA[52].

Adiponectin seems to have both catabolic and anabolic effects on pathological changes of several tissues/cells involved in the initiation and progression of OA. For its pro-inflammatory effect, adiponectin plus IL-1β treated chondrocytes and synovial fibroblasts lead to the induction of NO by inducing the expression of NOS2. Similarly, this adipokine also increases the production of key mediators in cartilage degeneration such as IL-6, IL-8, TNF-α, MMP-3, MMP-9, MCP-1 (monocyte chemo-attractant protein-1) and GRO (growth-related oncogene) in chondrocytes[53-55]

The stimulation of osteoblasts with adiponectin increased the production of the inflammatory mediators IL-6, IL-8, and MCP-1. In grade 1 (non-ossified) osteophytes, adiponectin were detectable in connective tissue fibroblasts. In grade 2–5 (ossified osteophytes) a lower extent of adiponectin was expressed by osteoblasts, suggesting its involvement in early osteophyte formation[56].

Plasma adiponectin levels showed positive associations with markers of cartilage degradation such as IL-1 β, uCTX-II and sCOMP, but showed negative associations with high sensitivity C-reactive protein (hsCRP) levels in serum. These associations turned stronger after adjustments for BMI. On the other hand, other studies have suggested positive associations between hsCRP and synovial fluid adiponectin in end-stage knee OA patients[20]. In addition, Kang et al. reported increased levels of collagen type II degradation products in supernatants of OA cartilage explants incubated with adiponectin[57].

Compared to less severely affected subjects, Koskinen et al. found increased plasma adiponectin levels in patients with grade 4-5 radiographic Ahlbäck scores[58]. In addition, a significant association between plasma adiponectin levels and the Lequesne index was found[59]. Filkova et al. also found that serum adiponectin levels were higher in erosive OA patients than in nonerosive OA patients[50]. However, Berry et al. did not find any association between baseline plasma adiponectin levels, cartilage volume changes and defects in knee OA subjects in a 2-year study[42].

Interestingly, several studies have shown a protective effect of adiponectin in knee OA. Chen et al. demonstrated down-regulated IL-1β induced MMP-13 production and up-regulated its associated inhibitor, TIMP-2 (tissue inhibitor of metalloproteinase-2), production in primary chondrocytes at both mRNA and protein levels, suggesting the protective role against cartilage damage[47]. Some clinical data also support that adiponectin could play a protective role against OA. Honsawek and Chayanupatkul showed an inverse correlation between plasma adiponectin and radiographic knee OA severity. They found increased adiponectin levels in grade 2 (KL-score) knee OA patients compared with controls, but decreased levels in grade 4 (KL-score) knee OA patients[60].

Visfatin

Visfatin, also called pre-B-cell colony-enhancing factor (PBEF) and nicotinamide phosphoribosyl transferase (NAMPT), is a highly conserved 52-kDa protein of 471 amino acids[61]. The major visfatin producing cells are granulocytes, monocytes and macrophages[62, 63]. It was originally discovered in human bone marrow, liver and muscle[61]. Additionally, adipocytes have also been considered as another source for visfatin production[64]. The best characteristic of visfatin is NAD biosynthetic enzyme[65]. It can bind to the insulin receptor *in vivo* and *in vitro*, but its insulin-mimetic effects are under investigation[66]. The elevated plasma visfatin levels have been found in type 2 and type 1 diabetes mellitus patients[67, 68]. It has recently been demonstrated that pharmacological inhibition of visfatin with APO866 (FK866), a NAD biosynthesis inhibitor , decreased collagen-induced arthritis (CIA) severity and pro-inflammatory cytokine production in affected joints[69].

Visfatin is highly produced in the adipose tissue with increased levels in obese people compared with lean people[64], and its level can be

reduced by regular exercise[68]. In general, visfatin synthesis is regulated by other factors such as glucocorticoids, TNF-α, IL-1β, IL-6, and growth hormone (GH), and its circulating-level positively correlates with IL-6 levels[70,71]. Very recently, Jurdana et al. reported no significant differences in serum visfatin concentrations between genders, however, it seems to be higher in women than in men[72].

OA patients had significantly higher plasma and synovial fluid concentrations of visfatin compared with controls, with levels in synovial fluid higher than paired serum samples[73]. It was showed that OA infrapatellar fat pads release higher amounts of visfatin than the matched subcutaneous adipose tissue[74]. Moreover, the visfatin expression in OA cartilage and the synovium was also higher than in normal samples[75].

The role of visfatin in cartilage is still unclear since it showed association with both catabolic and anabolic processes; however, more evidences point visfatin to be a pro-catabolic inflammatory, rather than anabolic mediator. For example, it has been shown that visfatin increased MMP activity and NO production, as well as proteoglycan release in OA cartilage matrix[76]. A recent study had shown that visfatin counteracted anabolic IGF-1 signaling, and therefore reduced IGF-1-mediated proteoglycan synthesis in human chondrocytes[77]. Moreover, elevated level of visfatin can reduce the expression of factors essential for the maintenance of the chondrocyte phenotype such as Sox-9 and type II collagen[78]. On the other hand, visfatin has also showed some anabolic properties. It was demonstrated that the inhibition of visfatin by small interfering RNA (siRNA) decreased the production of human chondrocyte specific matrix gene such as *collagen2a1* and *aggrecan*[79].

Visfatin is also expressed in osteoblasts, osteoclasts and osteophyte, suggesting its role in early osteophyte formation[56]. Plasma visfatin concentrations showed a positive correlation with CRP, indicating that it may be related to lipid metabolism and inflammatory process[70,80]. Likewise, synovial visfatin concentrations were shown positively correlated with the degradation biomarker of collagen type II, CTX-II, and two degradation biomarkers of aggrecan: AGG1 (G1-1H11), and AGG2 (6D6-G2)[81].

Resistin

Resistin is a macrophage/monocyte-derived adipokine which has an important role in inflammatory processes[82]. This dimeric protein is secreted mainly by adipocytes, but other cell types such as macrophages and neutrophils have been found to produce resistin as well[83]. The association of resistin with obesity, together with its proinflammatory properties suggests that resistin might be a remarkable mediator that links inflammation with OA and obesity.

Resistin levels in serum were significantly higher than the levels in matched synovial fluid specimens and increased in obese individuals[84]. This adipokine showed significantly higher levels in females than in males. Interestingly, serum resistin levels were positively associated with histologically determined grades of synovial inflammation[85]. It can be detected in inflamed synovium joints, in both rheumatoid arthritis (RA) and OA[29, 85]. Serum resistin levels in OA patients were positively associated with age, but not BMI and were significantly higher than in controls[20]. Resistin production can be induced by proinflammatory cytokines such as IL-1, IL-6 and TNF[86].

Resistin can induce inflammatory cytokines and PGE2 synthesis. It is produced by osteoblasts and osteoclasts in ossified osteophytes, indicating a role in osteophyte formation. Moreover, resistin stimulated proteoglycan degradation as well as inhibited proteoglycan production in mouse and human cartilage explants[87]. Plasma resistin concentrations were positively associated with sPIIINP and the prevalence of radiographic knee OA, independently with BMI; however, it was not associated with the disease progression. Interestingly, the association between resistin and the presence of radiographic knee OA was more obvious in OA patients with higher adiponectin levels[59].

Other Adipokines

Chemerin

Chemerin, a recently described chemo-attractant adipokine, is an18 kDa protein which is also known as tazarotene-induced gene 2 or retinoic acid receptor responder 2[88]. Its functions involved in adipocyte development and metabolic function, as well as glucose metabolism via the G coupled receptor chemokine-like receptor 1[89]. Chemerin and its receptor are mainly expressed in adipose tissue but can also be produced by dendritic cells, macrophages, fibroblast-like synoviocytes, and chondrocytes[90]. Molecules which drive inflammatory processes such as IL-1β, along with leptin and glucocorticoids, are able to modulate the expression of this adipokine[18]. Chemerin significantly increases the synthesis of Toll-like receptor 4 and CCL2 in OA fibroblast-like synoviocytes[91]. In addition, it stimulates the production of proinflammatory cytokines and matrix metalloproteinase in chondrocytes[92]. Moreover, chemerin levels in OA synovial fluid were associated with disease severity[93], demonstrating an important role of chemerin in OA pathophysiology.

Lipocalin

Lipocalin 2 (LCN2), a 25 kDa glycoprotein, is also named 24p3, uterocalin, siderocalin, and neutrophil gelatinase-associated lipocalin. It is a monomer adipokine produced mainly from adipose tissue and neutrophils but has recently been identified in chondrocytes[94]. It can exist as a 46 kDa homodimer and its cellular receptor named megalin (GP330)[95]. Its expression can be regulated by leptin, adiponectin, IL-1β, LPS, and dexamethasone[18]. This adipokine is likely to be involved in matrix degradation.

Omentin

Omentin is a 40 kDa protein which has previously been recognized as intelectin (a new form of Ca^{2+}-dependent lectin). It is secreted predominantly by omental adipose tissue and its plasma concentration is high. Several studies have shown the involvement of this adipokine in OA pathogenesis. For example, inflammatory states and obesity have been shown to alter omentin gene expression[96]. Recently, Senolt et al. found a difference in levels of omentin in the synovial fluid between RA and OA patients[97].

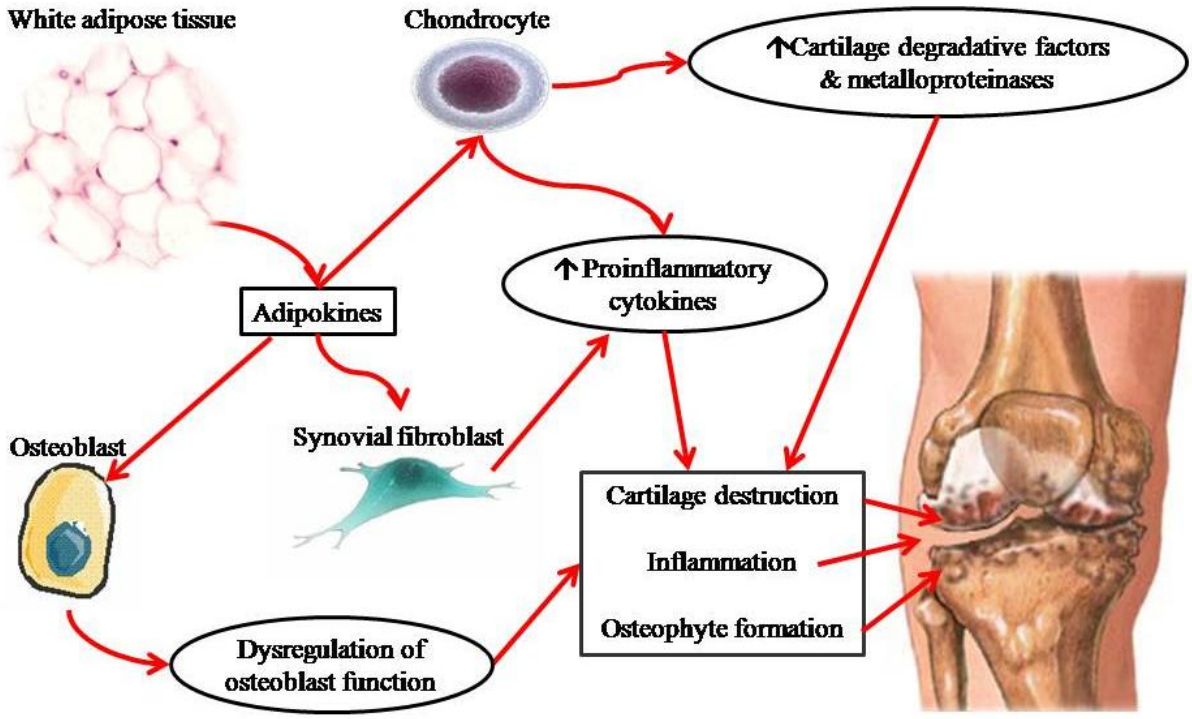


Fig. 1 Complex network links excess white adipose tissue, bone, and articular cartilage in knee osteoarthritis.

Conclusion

Taken together, this review sheds light on a potential role of adipokines in OA development as shown in Fig. 1. Leptin and visfatin seem to be more interesting as the targets of both prevention and treatment for knee osteoarthritis since they obviously showed catabolic effects on articular cartilage, whereas the effects of adiponectin and resistin are heterogenous. However, these two adipokines also play a crucial role in many other physiological processes, thus more clinical studies together with more research on the other adipokines are warranted. It is noteworthy that women have higher adipokines levels than men, which may be the reason for a higher prevalence of OA in women.

Obesity is undoubtedly associated with increased risk of knee OA. However, the use of BMI alone for measurement of excess body weight seems inadequate to reveal the physiological changes that link obesity to OA because it reflects both fat and skeletal muscle mass. The main source of adipokine production is adipose tissues, thus the other explicit measurements of body fat such as waist-hip circumference or Dual-energy X-ray absorptiometry-assessed total fat mass will be useful techniques to investigate the relationship between obesity, adipokine production and OA. Moreover, the study of interactions between metabolic factors and the other OA risk factors such as mechanical stress and genetic alteration, resulting from obesity may improve the understanding on the pathogenesis of OA.

Lastly, although the knowledge gained from present literatures is still incomplete for knee OA prevention and therapeutic intervention by pharmacological strategies, it is possible to state that an available preventive strategy is to stay in shape.

Acknowledgements

This work has been supported by Post-Doctoral Fellowship Research Grant from Ratchadaphiseksomphot Endowment Fund, Chulalongkorn University. The authors would like to thank Thomas Mabey for kindly reviewing the manuscript.

Conflict of interest

None

References

1. Dillon CF, Rasch EK, Gu Q, Hirsch R. Prevalence of knee osteoarthritis in the United States: arthritis data from the Third National Health and Nutrition Examination Survey 1991-94. J Rheumatol 2006; 33: 2271-9.
2. Felson DT. An update on the pathogenesis and epidemiology of osteoarthritis. Radiologic Clinics of North America 2004; 42: 1-9.
3. Salihu HM, Bonnema SM, Alio AP. Obesity: What is an elderly population growing into? Maturitas 2009; 63: 7-12.
4. Hochberg MC, Lethbridge-Cejku M, Scott WW, Jr., Reichle R, Plato CC, Tobin JD. The association of body weight, body fatness and body fat distribution with osteoarthritis of the knee: data from the Baltimore Longitudinal Study of Aging. J Rheumatol 1995; 22: 488-93.
5. Coggon D, Reading I, Croft P, McLaren M, Barrett D, Cooper C. Knee osteoarthritis and obesity. Int J Obes Relat Metab Disord 2001; 25: 622-7.
6. Hart DJ, Spector TD. The relationship of obesity, fat distribution and osteoarthritis in women in the general population: the Chingford Study. J Rheumatol 1993; 20: 331-5.
7. Lachance L, Sowers M, Jamadar D, Jannausch M, Hochberg M, Crutchfield M. The experience of pain and emergent osteoarthritis of the knee. Osteoarthritis Cartilage 2001; 9: 527-32.
8. Manninen P, Riihimaki H, Heliovaara M, Makela P. Overweight, gender and knee osteoarthritis. Int J Obes Relat Metab Disord 1996; 20: 595-7.
9. Grotle M, Hagen KB, Natvig B, Dahl FA, Kvien TK. Obesity and osteoarthritis in knee, hip and/or hand: an epidemiological study in the general population with 10 years follow-up. BMC Musculoskelet Disord 2008; 9: 132.
10. Yusuf E, Nelissen RG, Ioan-Facsinay A, Stojanovic-Susulic V, DeGroot J, van Osch G, et al. Association between weight or body mass index and hand osteoarthritis: a systematic review. Ann Rheum Dis 2010; 69: 761-5.
11. Pottie P, Presle N, Terlain B, Netter P, Mainard D, Berenbaum F. Obesity and osteoarthritis: more complex than predicted! Ann Rheum Dis 2006; 65: 1403-5.
12. Conrozier T, Chappuis-Cellier C, Richard M, Mathieu P, Richard S, Vignon E. Increased serum C-reactive protein levels by immunonephelometry in patients with rapidly destructive hip osteoarthritis. Rev Rhum Engl Ed 1998; 65: 759-65.
13. Spector TD, Hart DJ, Nandra D, Doyle DV, Mackillop N, Gallimore JR, et al. Low-level increases in serum C-reactive protein are present in early osteoarthritis of the knee and predict progressive disease. Arthritis Rheum 1997; 40: 723-7.
14. Goldring MB, Otero M. Inflammation in osteoarthritis. Curr Opin Rheumatol 2011; 23: 471-8.
15. Katz JD, Agrawal S, Velasquez M. Getting to the heart of the matter: osteoarthritis takes its place as part of the metabolic syndrome. Curr Opin Rheumatol 2010; 22: 512-9.
16. Hotamisligil GS, Shargill NS, Spiegelman BM. Adipose expression of tumor necrosis factor-alpha: direct role in obesity-linked insulin resistance. Science 1993; 259: 87-91.
17. Fantuzzi G. Adiponectin and inflammation: consensus and controversy. J Allergy Clin Immunol 2008; 121: 326-30.
18. Conde J, Gomez R, Bianco G, Scotece M, Lear P, Dieguez C, et al. Expanding the adipokine network in cartilage: identification and regulation of novel factors in human and murine chondrocytes. Ann Rheum Dis 2011; 70: 551-9.
19. Gualillo O, Gonzalez-Juanatey JR, Lago F. The emerging role of adipokines as mediators of cardiovascular function: physiologic and clinical perspectives. Trends Cardiovasc Med 2007; 17: 275-83.
20. de Boer TN, van Spil WE, Huisman AM, Polak AA, Bijlsma JW, Lafeber FP, et al. Serum adipokines in osteoarthritis; comparison with controls and relationship with local parameters of synovial inflammation and cartilage damage. Osteoarthritis Cartilage 2012; 20: 846-53.
21. Zhang Y, Proenca R, Maffei M, Barone M, Leopold L, Friedman JM. Positional cloning of the mouse obese gene and its human homologue. Nature 1994; 372: 425-32.
22. Henry BA, Clarke IJ. Adipose tissue hormones and the regulation of food intake. J Neuroendocrinol 2008; 20: 842-9.
23. Gualillo O, Eiras S, Lago F, Dieguez C, Casanueva FF. Elevated serum leptin concentrations induced by experimental acute inflammation. Life Sci 2000; 67: 2433-41.
24. Tartaglia LA, Dembski M, Weng X, Deng N, Culpepper J, Devos R, et al. Identification and expression cloning of a leptin receptor, OB-R. Cell 1995; 83: 1263-71.
25. Fruhbeck G. Intracellular signalling pathways activated by leptin. Biochemical Journal 2006; 393: 7-20.

26. Tilg H, Moschen AR. Adipocytokines: mediators linking adipose tissue, inflammation and immunity. Nat Rev Immunol 2006; 6: 772-83.
27. Bernotiene E, Palmer G, Talabot-Ayer D, Szalay-Quinodoz I, Aubert ML, Gabay C. Delayed resolution of acute inflammation during zymosan-induced arthritis in leptin-deficient mice. Arthritis Research & Therapy 2004; 6: R256-R63.
28. Gegout PP, Francin PJ, Mainard D, Presle N. Adipokines in osteoarthritis: friends or foes of cartilage homeostasis? Joint Bone Spine 2008; 75: 669-71.
29. Presle N, Pottie P, Dumond H, Guillaume C, Lapicque F, Pallu S, et al. Differential distribution of adipokines between serum and synovial fluid in patients with osteoarthritis. Contribution of joint tissues to their articular production. Osteoarthritis Cartilage 2006; 14: 690-5.
30. Dumond H, Presle N, Terlain B, Mainard D, Loeuille D, Netter P, et al. Evidence for a key role of leptin in osteoarthritis. Arthritis Rheum 2003; 48: 3118-29.
31. Karvonen-Gutierrez CA, Harlow S. Leptin Levels Are Associated with Knee Osteoarthritis among Mid-Aged Women. Osteoarthritis and Cartilage 2012; 20: S189-S90.
32. Hu PF, Bao JP, Wu LD. The emerging role of adipokines in osteoarthritis: a narrative review. Mol Biol Rep 2011; 38: 873-8.
33. Toussirot E, Streit G, Wendling D. The contribution of adipose tissue and adipokines to inflammation in joint diseases. Curr Med Chem 2007; 14: 1095-100.
34. Bao JP, Chen WP, Feng J, Hu PF, Shi ZL, Wu LD. Leptin plays a catabolic role on articular cartilage. Molecular Biology Reports 2010; 37: 3265-72.
35. Otero M, Gomez Reino JJ, Gualillo O. Synergistic induction of nitric oxide synthase type II: in vitro effect of leptin and interferon-gamma in human chondrocytes and ATDC5 chondrogenic cells. Arthritis Rheum 2003; 48: 404-9.
36. Gomez R, Scotece M, Conde J, Gomez-Reino JJ, Lago F, Gualillo O. Adiponectin and leptin increase IL-8 production in human chondrocytes. Ann Rheum Dis 2011; 70: 2052-4.
37. Simopoulou T, Malizos KN, Iliopoulos D, Stefanou N, Papatheodorou L, Ioannou M, et al. Differential expression of leptin and leptin's receptor isoform (Ob-Rb) mRNA between advanced and minimally affected osteoarthritic cartilage; effect on cartilage metabolism. Osteoarthritis Cartilage 2007; 15: 872-83.
38. Steppan CM, Crawford DT, Chidsey-Frink KL, Ke HZ, Swick AG. Leptin is a potent stimulator of bone growth in ob/ob mice. Regulatory Peptides 2000; 92: 73-8.
39. Kume K, Satomura K, Nishisho S, Kitaoka E, Yamanouchi K, Tobiume S, et al. Potential role of leptin in endochondral ossification. J Histochem Cytochem 2002; 50: 159-69.
40. Gordeladze JO, Drevon CA, Syversen U, Reseland JE. Leptin stimulates human osteoblastic cell proliferation, de novo collagen synthesis, and mineralization: Impact on differentiation markers, apoptosis, and osteoclastic signaling. J Cell Biochem 2002; 85: 825-36.
41. Mutabaruka MS, Aoulad Aissa M, Delalandre A, Lavigne M, Lajeunesse D. Local leptin production in osteoarthritis subchondral osteoblasts may be responsible for their abnormal phenotypic expression. Arthritis Res Ther 2010; 12: R20.
42. Berry PA, Jones SW, Cicuttini FM, Wluka AE, Maciewicz RA. Temporal relationship between serum adipokines, biomarkers of bone and cartilage turnover, and cartilage volume loss in a population with clinical knee osteoarthritis. Arthritis Rheum 2011; 63: 700-7.
43. Ouchi N, Shibata R, Walsh K. Cardioprotection by adiponectin. Trends in Cardiovascular Medicine 2006; 16: 141-6.
44. Matsuzawa Y. Adiponectin: Identification, physiology and clinical relevance in metabolic and vascular disease. Atherosclerosis Supplements 2005; 6: 7-14.
45. Kadowaki T, Yamauchi T. Adiponectin and adiponectin receptors. Endocrine Reviews 2005; 26: 439-51.
46. Yamauchi T, Kamon J, Ito Y, Tsuchida A, Yokomizo T, Kita S, et al. Cloning of adiponectin receptors that mediate antidiabetic metabolic effects. Nature 2003; 423: 762-9.
47. Chen TH, Chen L, Hsieh MS, Chang CP, Chou DT, Tsai SH. Evidence for a protective role for adiponectin in osteoarthritis. Biochim Biophys Acta 2006; 1762: 711-8.
48. Oh DK, Ciaraldi T, Henry RR. Adiponectin in health and disease. Diabetes Obes Metab 2007; 9: 282-9.
49. Cnop M, Havel PJ, Utzschneider KM, Carr DB, Sinha MK, Boyko EJ, et al. Relationship of adiponectin to body fat distribution, insulin sensitivity and plasma lipoproteins: evidence for independent roles of age and sex. Diabetologia 2003; 46: 459-69.
50. Filkova M, Liskova M, Hulejova H, Haluzik M, Gatterova J, Pavelkova A, et al. Increased serum adiponectin levels in female patients with erosive compared with non-erosive osteoarthritis. Ann Rheum Dis 2009; 68: 295-6.
51. Laurberg TB, Frystyk J, Ellingsen T, Hansen IT, Jorgensen A, Tarp U, et al. Plasma adiponectin in patients with active, early, and chronic

rheumatoid arthritis who are steroid- and disease-modifying antirheumatic drug-naive compared with patients with osteoarthritis and controls. J Rheumatol 2009; 36: 1885-91.
52. Distel E, Cadoudal T, Durant S, Poignard A, Chevalier X, Benelli C. The infrapatellar fat pad in knee osteoarthritis: an important source of interleukin-6 and its soluble receptor. Arthritis Rheum 2009; 60: 3374-7.
53. Tang CH, Chiu YC, Tan TW, Yang RS, Fu WM. Adiponectin enhances IL-6 production in human synovial fibroblast via an AdipoR1 receptor, AMPK, p38, and NF-kappa B pathway. J Immunol 2007; 179: 5483-92.
54. Lago R, Gomez R, Otero M, Lago F, Gallego R, Dieguez C, et al. A new player in cartilage homeostasis: adiponectin induces nitric oxide synthase type II and pro-inflammatory cytokines in chondrocytes. Osteoarthritis Cartilage 2008; 16: 1101-9.
55. Tong KM, Chen CP, Huang KC, Shieh DC, Cheng HC, Tzeng CY, et al. Adiponectin increases MMP-3 expression in human chondrocytes through AdipoR1 signaling pathway. J Cell Biochem 2011; 112: 1431-40.
56. Junker S, Frommer KW, Krumbholz G, Lehr A, Rehart S, Steinmeyer J, et al. Expression of adipocytokines in osteoarthritis osteophytes. Osteoarthritis and Cartilage 2012; 20S1: S115.
57. Kang EH, Lee YJ, Kim TK, Chang CB, Chung JH, Shin K, et al. Adiponectin is a potential catabolic mediator in osteoarthritis cartilage. Arthritis Res Ther 2010; 12: R231.
58. Koskinen A, Juslin S, Nieminen R, Moilanen T, Vuolteenaho K, Moilanen E. Adiponectin associates with markers of cartilage degradation in osteoarthritis and induces production of proinflammatory and catabolic factors through mitogen-activated protein kinase pathways. Arthritis Res Ther 2011; 13: R184.
59. Van Spil WE, Welsing PM, Kloppenburg M, Bierma-Zeinstra SM, Bijlsma JW, Mastbergen SC, et al. Cross-sectional and predictive associations between plasma adipokines and radiographic signs of early-stage knee osteoarthritis: data from CHECK. Osteoarthritis Cartilage 2012; 20: 1278-85.
60. Honsawek S, Chayanupatkul M. Correlation of plasma and synovial fluid adiponectin with knee osteoarthritis severity. Arch Med Res 2010; 41: 593-8.
61. Samal B, Sun YH, Stearns G, Xie CS, Suggs S, Mcniece I. Cloning and Characterization of the Cdna-Encoding a Novel Human Pre-B-Cell Colony-Enhancing Factor. Molecular and Cellular Biology 1994; 14: 1431-7.
62. Friebe D, Neef M, Kratzsch J, Erbs S, Dittrich K, Garten A, et al. Leucocytes are a major source of circulating nicotinamide phosphoribosyltransferase (NAMPT)/pre-B cell colony (PBEF)/visfatin linking obesity and inflammation in humans. Diabetologia 2011; 54: 1200-11.
63. Curat CA, Wegner V, Sengenes C, Miranville A, Tonus C, Busse R, et al. Macrophages in human visceral adipose tissue: increased accumulation in obesity and a source of resistin and visfatin. Diabetologia 2006; 49: 744-7.
64. Fukuhara A, Matsuda M, Nishizawa M, Segawa K, Tanaka M, Kishimoto K, et al. Visfatin: A protein secreted by visceral fat that mimics the effects of insulin (Retracted article, see vol 318, pg 565, 2007). Science 2005; 307: 426-30.
65. Wang T, Zhang X, Bheda P, Revollo JR, Imai SI, Wolberger C. Structure of Nampt/PBEF/visfatin, a mammalian NAD(+) biosynthetic enzyme. Nature Structural & Molecular Biology 2006; 13: 661-2.
66. Normile D. Scientific publishing - Osaka University researchers reject demand to retract Science paper. Science 2007; 316: 1681.
67. Chen MP, Chung FM, Chang DM, Tsai JCR, Huang HF, Shin SJ, et al. Elevated plasma level of visfatin/pre-B cell colony-enhancing factor in patients with type 2 diabetes mellitus. Journal of Clinical Endocrinology & Metabolism 2006; 91: 295-9.
68. Haider DG, Pleiner J, Francesconi M, Wiesinger GF, Muller M, Wolzt M. Exercise training lowers plasma visfatin concentrations in patients with type 1 diabetes. Journal of Clinical Endocrinology & Metabolism 2006; 91: 4702-4.
69. Busso N, Karababa M, Nobile M, Rolaz A, Van Gool F, Galli M, et al. Pharmacological Inhibition of Nicotinamide Phosphoribosyltransferase/Visfatin Enzymatic Activity Identifies a New Inflammatory Pathway Linked to NAD. PLoS One 2008; 3.
70. Auguet T, Terra X, Porras JA, Orellana-Gavalda J, Martinez S, Aguilar C, et al. Plasma visfatin levels and gene expression in morbidly obese women with associated fatty liver disease. Clinical Biochemistry 2013; 46: 202-8.
71. Mazaherioun M, Hosseinzadeh-Attar MJ, Janani L, Farahani AV, Rezvan N, Karbaschian Z, et al. Elevated Serum Visfatin Levels in Patients with Acute Myocardial Infarction. Archives of Iranian Medicine 2012; 15: 688-92.
72. Jurdana M, Petelin A, Černelič Bizjak M, Bizjak M, Biolo G, Jenko-Pražnikar Z. Increased serum visfatin levels in obesity and its association with anthropometric/biochemical parameters, physical inactivity and nutrition. e-SPEN Journal 2013; 8: e59-e67.
73. Chen WP, Bao JP, Feng J, Hu PF, Shi ZL, Wu LD. Increased serum concentrations of visfatin and its production by different joint tissues in patients with osteoarthritis. Clinical Chemistry and Laboratory Medicine 2010; 48: 1141-5.

74. Klein-Wieringa IR, Kloppenburg M, Bastiaansen-Jenniskens YM, Yusuf E, Kwekkeboom JC, El-Bannoudi H, et al. The infrapatellar fat pad of patients with osteoarthritis has an inflammatory phenotype. Ann Rheum Dis 2011; 70: 851-7.
75. Gosset M, Berenbaum F, Salvat C, Sautet A, Pigenet A, Tahiri K, et al. Crucial role of visfatin/pre-B cell colony-enhancing factor in matrix degradation and prostaglandin E-2 synthesis in chondrocytes. Arthritis and Rheumatism 2008; 58: 1399-409.
76. McNulty AL, Miller MR, O'Connor SK, Guilak F. The effects of adipokines on cartilage and meniscus catabolism. Connect Tissue Res 2011; 52: 523-33.
77. Yammani RR, Loeser RF. Extracellular nicotinamide phosphoribosyltransferase (NAMPT/visfatin) inhibits insulin-like growth factor-1 signaling and proteoglycan synthesis in human articular chondrocytes. Arthritis Res Ther 2012; 14: R23.
78. Hong EH, Yun HS, Kim J, Um HD, Lee KH, Kang CM, et al. Nicotinamide phosphoribosyltransferase is essential for interleukin-1beta-mediated dedifferentiation of articular chondrocytes via SIRT1 and extracellular signal-regulated kinase (ERK) complex signaling. J Biol Chem 2011; 286: 28619-31.
79. Dvir-Ginzberg M, Gagarina V, Lee EJ, Hall DJ. Regulation of cartilage-specific gene expression in human chondrocytes by SirT1 and nicotinamide phosphoribosyltransferase. J Biol Chem 2008; 283: 36300-10.
80. Lago F, Dieguez C, Gomez-Reino J, Gualillo O. Adipokines as emerging mediators of immune response and inflammation. Nat Clin Pract Rheumatol 2007; 3: 716-24.
81. Duan Y, Hao D, Li M, Wu Z, Li D, Yang X, et al. Increased synovial fluid visfatin is positively linked to cartilage degradation biomarkers in osteoarthritis. Rheumatol Int 2012; 32: 985-90.
82. Steppan CM, Lazar MA. Resistin and obesity-associated insulin resistance. Trends Endocrinol Metab 2002; 13: 18-23.
83. Conde J, Scotece M, Gomez R, Lopez V, Gomez-Reino JJ, Gualillo O. Adipokines and osteoarthritis: novel molecules involved in the pathogenesis and progression of disease. Arthritis 2011; 2011: 203901.
84. Degawa-Yamauchi M, Bovenkerk JE, Juliar BE, Watson W, Kerr K, Jones R, et al. Serum resistin (FIZZ3) protein is increased in obese humans. J Clin Endocrinol Metab 2003; 88: 5452-5.
85. Senolt L, Housa D, Vernerova Z, Jirasek T, Svobodova R, Veigl D, et al. Resistin in rheumatoid arthritis synovial tissue, synovial fluid and serum. AnnRheumDis2007;66:458-63.
86. Kaser S, Kaser A, Sandhofer A, Ebenbichler CF, Tilg H, Patsch JR. Resistin messenger-RNA expression is increased by proinflammatory cytokines in vitro. Biochem Biophys Res Commun 2003; 309: 286-90.
87. Lee JH, Ort T, Ma K, Picha K, Carton J, Marsters PA, et al. Resistin is elevated following traumatic joint injury and causes matrix degradation and release of inflammatory cytokines from articular cartilage in vitro. Osteoarthritis Cartilage 2009; 17: 613-20.
88. Wittamer V, Franssen JD, Vulcano M, Mirjolet JF, Le Poul E, Migeotte I, et al. Specific recruitment of antigen-presenting cells by chemerin, a novel processed ligand from human inflammatory fluids. Journal of Experimental Medicine 2003; 198: 977-85.
89. Ernst MC, Sinal CJ. Chemerin: at the crossroads of inflammation and obesity. Trends Endocrinol Metab 2010; 21: 660-7.
90. Bozaoglu K, Bolton K, McMillan J, Zimmet P, Jowett J, Collier G, et al. Chemerin is a novel adipokine associated with obesity and metabolic syndrome. Endocrinology 2007; 148: 4687-94.
91. Eisinger K, Bauer S, Schaffler A, Walter R, Neumann E, Buechler C, et al. Chemerin induces CCL2 and TLR4 in synovial fibroblasts of patients with rheumatoid arthritis and osteoarthritis. Exp Mol Pathol 2012; 92: 90-6.
92. Berg V, Sveinbjornsson B, Bendiksen S, Brox J, Meknas K, Figenschau Y. Human articular chondrocytes express ChemR23 and chemerin; ChemR23 promotes inflammatory signalling upon binding the ligand chemerin(21-157). Arthritis Res Ther 2010; 12: R228.
93. Huang K, Du G, Li L, Liang H, Zhang B. Association of chemerin levels in synovial fluid with the severity of knee osteoarthritis. Biomarkers 2012; 17: 16-20.
94. Owen HC, Roberts SJ, Ahmed SF, Farquharson C. Dexamethasone-induced expression of the glucocorticoid response gene lipocalin 2 in chondrocytes. Am J Physiol Endocrinol Metab 2008; 294: E1023-34.
95. Hvidberg V, Jacobsen C, Strong RK, Cowland JB, Moestrup SK, Borregaard N. The endocytic receptor megalin binds the iron transporting neutrophil-gelatinase-associated lipocalin with high affinity and mediates its cellular uptake. FEBS Lett 2005; 579: 773-7.
96. De Souza Batista CM, Yang RZ, Lee MJ, Glynn NM, Yu DZ, Pray J, et al. Omentin plasma levels and gene expression are decreased in obesity. Diabetes 2007; 56: 1655-61.
97. Senolt L, Polanska M, Filkova M, Cerezo LA, Pavelka K, Gay S, et al. Vaspin and omentin: new adipokines differentially regulated at the site of inflammation in rheumatoid arthritis. Ann Rheum Dis 2010; 69: 1410-1.

ความสำคัญของอดิโพไคน์กับความเชื่อมโยงระหว่างโรคข้อเข่าเสื่อมและโรคอ้วน

ธิติยา พูลเพ็ชร์, ปรด, สิทธิศักดิ์ หรรษาเวก, พบ

โรคข้อเสื่อมเป็นโรคข้อที่เกิดจากการเสื่อมสภาพอย่างเรื้อรังของกระดูกอ่อนผิวข้อ กระดูกใต้ชั้นกระดูกอ่อน เยื่อหุ้มข้อ ตลอดจนกล้ามเนื้อและเส้นเอ็น เนื่องมาจากสาเหตุหลายประการ โรคอ้วนเป็นหนึ่งในปัจจัยเสี่ยงที่สำคัญและมีส่วนเกี่ยวข้องกับอุบัติการณ์และความชุกของโรคข้อเสื่อม และเชื่อว่ามีบทบาทอย่างมากต่อกระบวนการเกิดโรคข้อเข่าเสื่อม โดยมีผลไปเพิ่มความเค้นเชิงกลต่อข้อ บทบาทของโรคอ้วนในโรคข้อเข่าเสื่อมมีความซับซ้อนมากและเกี่ยวข้องกับไซโตไคน์อดิโพไคน์ (adipokines) จัดเป็นไซโตไคน์ชนิดหนึ่งซึ่งถูกสร้างขึ้นมาจากเนื้อเยื่อไขมันเป็นหลัก และมีบทบาทสำคัญมากต่อโรคข้อเข่าเสื่อม บทความปริทรรศน์นี้ได้รวบรวมความรู้ความก้าวหน้าอันทันสมัยจากการศึกษาวิจัยอดิโพไคน์ในโรคข้อเข่าเสื่อม โดยมุ่งเน้นถึงเลปติน (leptin) อดิโพเนคติน (adiponectin) วิสฟาติน (visfatin) และรีซิสติน (resistin) รวมถึงเคเมริน (chemerin) ไลโพคาลิน (lipocalin) และโอเมนติน (omentin)

Mesenchymal Stem Cells for Regeneration of Cartilage Lesions:

Focus on knee osteoarthritis

Baldur Kristjánsson, MS[1], Thomas Mabey, BS[1], Pongsak Yuktanandana, MD[2], Vinai Parkpian, MD[2], Sittisak Honsawek, MD[1,2]

[1]*Department of Biochemistry, Faculty of Medicine, Chulalongkorn University, King Chulalongkorn Memorial Hospital, Thai Red Cross Society, Bangkok, Thailand*

[2]*Department of Orthopaedics, Faculty of Medicine, Chulalongkorn University, King Chulalongkorn Memorial Hospital, Thai Red Cross Society, Bangkok, Thailand*

With an increase in life expectancy which causes an ageing population, osteoarthritis, including cartilage loss and other cartilage lesions can become a major health problem. Cartilage has little self-renewal or regeneration capacity and those with cartilage lesions suffer from slow degeneration of the cartilage resulting in pain and loss of function. Conventional treatment for cartilage lesions often results in little or no pain relief leaving major surgery as the only viable option for improving the quality of life. Even so, available surgeries are not a permanent relief of the condition nor do they reverse the process of cartilage degeneration. Limited research funding, low public attention and a poor understanding of the mechanisms behind the conditions are several reasons that contribute to the lack of progress in developing treatments for cartilage degenerative conditions. In addition, cartilage degeneration is usually a slow process and early detection is often difficult due to the lack of biomarkers. In recent years, new methods have been suggested such as the use of autologous mesenchymal stem cells as a treatment of conditions like osteoarthritis. Clinical trials in both animal and human models have shown good results suggesting a simple, effective and lasting solution for cartilage lesions might be around the corner.

The Thai Journal of Orthopaedic Surgery: 37 No.2-4: 67-78
Full text. e journal: *http://www.rcost.or.th, http://thailand.digitaljournals.org/index.php/JRCOST*

Introduction

Osteoarthritis (OA) is a pathologic process of degenerative joint disease affecting all joints, though most commonly occurring in the hand, knee, and hip[(1)]. It is the most prevalent chronic joint disease with knee OA being a common form with a high prevalence in Asian countries[(2)]. Characteristics of the condition are damage to the articular cartilage, changes in the subchondral bone and synovium, followed by damage to the underlying bone and morphological changes such as subchondral sclerosis, subchondral bone cysts, osteophyte formation and synovitis[(3-5)]. Risk factors for osteoarthritis include a genetic predisposition, hereditary factors, obesity, age, mechanical injury, joint trauma, gender, joint immobilization, and overuse of the joint[(6,7)]. OA does not only cause disability but has been linked with other conditions such as neuropathic pain, depression, and sleep disorders[(8)]. Therefore, it has a great impact on society and is an economic burden responsible for up to 2% of all public health expenses[(9,10)]. Although OA is a common disease, no approved medical treatment exists to improve or reverse the articular cartilage damage[(11)]. Some controversial medications that suppress interleukin 1 and metalloproteinase, and stimulate transforming growth factor-β (TGF-β) may stop or reverse the process but have not been approved as a medical treatment yet. Frequently used treatments include physical therapy[(12)], pain control with steroidal and non-steroidal anti-inflammatory drugs, viscosupplementation with injections of sodium hyaluronan as well as a variety of nutraceuticals[(13)], however, none of these treatments have an impact on the progression of the condition. Although cell therapy by surgically implanting autologous chondrocytes has been used to regenerate cartilage damage for over two decades, the repair process is slow and often insufficient due to the poor self-renewal and regeneration abilities of the chondrocytes[(14,15)]. Therefore, the only treatment

Correspondence to: Honsawek S, Department of Biochemistry and Orthopaedics, Faculty of Medicine, Chulalongkorn University and King Chulalongkorn Memorial Hospital, Thai Red Cross Society, Rama IV road, Patumwan, Bangkok, 10330, Thailand
E-mail: sittisak.h@chula.ac.th

resulting in a quick relief of the condition is total joint replacement[13]. Total joint replacement is a major surgical procedure with risks of infections as well as the costs of hospital care, physiotherapy and rehabilitation[16]; it is therefore only used as a method of last resort. Other less invasive and cheaper methods have been suggested such as the use of stem cells. Mesenchymal stem cells have shown chondrogenic potential *in vitro* and might therefore provide an alternative treatment of damaged cartilage[17-19].

Mesenchymal stem cells

Mesenchymal stem cells (MSCs) are pluripotent progenitor cells. They are capable of establishing colonies from a single cell referred to as colony-forming fibroblast units. They were first described by Alexander Friedenstein as progenitor cells of bone and cartilage in 1966[20]. Since then they have been shown to have the capacity to differentiate into a variety of cell types including osteoblasts, chondrocytes, adipocytes, and myocytes[21]. They have also been shown to differentiate into nerve cells and hepatocytes which are normally derived from the other two major embryonic germ layers; the ectoderm and endoderm[22,23]. This is known as transdifferentiation or plasticity and MSCs can be considered as a source for more than just mesenchymal tissues[24,25]. MSCs are involved in the maintenance and regeneration of connective tissue and are known to migrate to tissues as a result of inflammation or injury where they participate in the repair of damage[26,27]. They are immunoprivileged cells with immunosuppressive properties[28]. In addition, MSCs are known to produce a number of secreted factors for example cytokines, chemokines, and growth factors[29-31]. MSCs therefore have considerable potential for tissue engineering.

Unlike the highly controversial embryonic stem cells, the MSCs are adult stem cells. They can be found in many tissues and organs but reside mainly within the bone-marrow. Bone-marrow derived mesenchymal stem cells (BMSCs) are therefore a widely used and well-studied cell line. Other common sources include adipose tissues, skeletal muscles, umbilical cord blood and Wharton's Jelly[32-34]. All of which have the capacity of differentiating into the cell lineages previously mentioned with BMSCs additionally being able to provide the stromal support system for haematopoietic stem cells[35]. Due to the abundance and distribution of MSCs in adult tissue, a patient's own MSCs can be isolated, expanded, and used as an autologous cell line. Not only does it eliminate the risk of host rejection but also the ethical concerns since the use of autologous cells is a generally accepted practice. When expanding MSCs *in vitro*, they are allowed to pass through stages known as "passage". Cells are usually let through 2-5 passages but it is not recommended that they pass through 10 or more due to the risk of mutations and tumor genetic effects. Indeed, one of the disadvantages of MSCs is their potential to give rise to or support tumors. In the literature, there exists controversial information with reports of tumor growth suppression as well as both increases and decreases in tumor growth.

Transplantations into immunodeficient animals have shown no evidence of tumor formation[36]. In 2011 Suzuki et al. showed that MSCs can support tumor growth by supporting the growth of the tumor stroma. They observed a significant increase in tumor growth when co-injecting mice with tumor cells and MSCs. However, their results were also controversial since they observed no increased tumor growth when using a different MSC line[37]. Therefore, the possibility of tumor development cannot be rejected completely when using MSCs.

Mesenchymal stem cells in joints

Synovial MSCs can be found in most tissues of the synovial joints in mammals. In humans they were first described by De Bari et al. when they successfully isolated MSCs from the synovial membrane in 2001[38]. Since then they have also been found in the meniscus, ligament, fat pad, cartilage and bone marrow of the synovial joints[39-43]. These cells have the capability of self-renewal and differentiation pathways similar to that of the BMCSs. MSCs from synovial fluid exhibit greater clonogenicity and chondrogenic capacity than those from bone marrow. They also show clonal heterogeneity with individual clonal populations exhibiting variable proliferation and differentiation potentials[44].

Since MSCs can be found in most tissues of the synovial joints it is likely that they must play a role in providing a reservoir of repair cells that can be activated for growth, repair or remodeling. They might also function as immunomodulatory sentinels for reducing inflammation or the activity of T-cells[45]. MSCs found in cartilage appear to lack the ability of functional repair since it is well known that cartilage fails to regenerate following injury. It is possible that MSCs in the cartilage serve a different purpose for example replenishing the surface zone proteoglycan lubricant to minimize friction[46].

A significantly greater number of MSCs can be recovered from the effected joints of OA or rheumatoid arthritis patients as well as those of ligament injury compared with that from healthy joints. The number of MSCs also increases with the severity of the disease and one hypothesis suggests that they originate in the degrading synovium[47]. In 2002, Murph et al. showed that MSCs from patients with end-stage OA had reduced *in vitro*

proliferation and differentiation potentials. They compared BMSCs from patients who underwent joint replacement surgery and compared them with samples from matched healthy individuals. They observed a significantly reduced yield and proliferation activity with cells having reduced chondrogenic and adipogenic activity and increased osteogenic potentials[48]. It has been shown that these functional deficiencies can be improved with supplementation of the medium with growth factors[49].

Availability and safety of MSCs

Obtaining cells for tissue engineering can be a major technical issue. It is possible to use allogeneic cells from donors but this is not common clinical practice due to the risk of rejection or disease transmission[50]. The use of autologous cells is considered safe because there is neither an immunological reaction nor the risk of disease transmission. However, using autologous cells also has limitations; availability may be scarce and it is important to select a tissue which results in minimal morbidity for the patient[51]. Autologous BMSCs are widely used because they can be easily obtained causing minimum morbidity and can be collected without producing tissue defects[52]. The yield obtained from bone-marrow can be quite low and cells are usually expanded *in vitro*. The cells are confirmed as MSCs by checking for surface markers commonly found on MSCs such as CD90 and CD105. Another good source for MSCs is adipose tissue. The number of cells that can be harvested from adipose tissue has been estimated to be up to 1,000 times greater than that from bone-marrow making it a good source for stem cells[53]. Obtaining adipose derived mesenchymal stem cells (AMSCs) is relatively simple with the use of liposuction where fat-pads are the major harvest sites. Like the harvesting of BMSCs, this technique causes minimal morbidity and is considered a safe method. Other sources of MSCs have been suggested but limited availability and difficulties in extraction have made BMSCs the most commonly used source for clinical application with AMSCs being investigated as a new more potent source of cells. Overall, it is hard to determine the safety of using autologous MSCs, although the risks of rejection or disease transfer is almost non-existent, the long-term effects have not yet been fully studied and the risk of tumor formation exists.

MSCs for cartilage repair

Most reports on the use of MSCs to treat cartilage defects focus on the use of BMSCs and a small number investigating AMSCs. Synovium derived mesenchymal stem cells (SMSCs) have been suggested for cartilage repair since some *in vitro* and animal studies have shown SMSCs to have a greater chondrogenic potential than BMSCs[54,55]. So far, there have been no clinical trials for this cell source in humans and harvesting SMSCs requires the use of arthroscopy which is more invasive than obtaining BMSCs[56].

Shigeyuki Wakitani is a pioneer in the field of cartilage repair using MSCs. In 1998 he and his team transplanted BMSCs to repair articular cartilage which was the first such clinical trial ever reported[57]. They performed this procedure on 40 more patients and published the first comprehensive study on the safety, effectiveness, and long-term effects of MSC transplantations for cartilage repair[58]. Their study was a long-term follow up study which included 41 patients with 45 joints and a follow up time of up to 11 years and 5 months. They harvested BMSCs from the iliac crest and expanded them in culture. The cells were delivered with surgery through a gel-cell composite or with the use of collagen sheets[57,59]. The surgeries were performed between January 1998 and November 2008 and the follow up time varied from 5 to 137 months. Of the 41 patients operated on, they were able to follow up on 31. There were no reports of tumor formation or infections over their follow up period. Therefore, they concluded that the use of BMSCs was an effective and safe way of treating cartilage defects. Although they had a long follow up period, the potential risk of tumor formation from stem cells should not be underestimated. Animal studies showed tumor formation or increased tumor proliferation as a result of introducing MSCs into the animals[60,61].

Autologous chondrocyte implantation for cartilage repair

Autologous chondrocyte implantation (ACI) has been suggested as a promising method for cartilage repair. Many comparative studies have shown promising results and in 2005 Fu et al. reported a significantly greater improvement in function and pain relieve in patients who received ACI treatment compared to those treated with debridement of cartilage defects in the knee[62]. MSCs have been shown to differentiate into chondrocytes or prevent cartilage degeneration and have therefore been suggested as an alternative cell source for cartilage repair[63]. By co-culturing MSCs and chondrocytes, Aung et al. were able to differentiate MSCs into chondrocytes without the use of growth factors and at the same time preventing their hypertrophic differentiation[64].

In 2010, Nejadnik et al. published a paper comparing the use of autologous BMSCs and autologous chondrocytes for treatment of cartilage defects[56]. The chondrocytes were harvested in surgery from non-weight bearing cartilage tissue and expanded in cultures. The BMSCs were harvested from the iliac crest using needle and likewise expanded in cultures. To confirm their

culture indeed existed of MSCs, they checked for cell surface markers commonly found on MSCs.
Cell sheets were produced for both chondrocytes and BMSCs by culturing the cells in the presence of ascorbic acid. For each surgery, at least 4 cells sheets were prepared with a cell density of 2 x 10^6 cells/cm^2. After cell harvest and expansion, patients underwent ACI surgery[15] and received either a chondrocyte or BMSC sheet implant of approximately 1-1.5 x 10^6 cells. Patients were evaluated preoperatively and at 3, 6, 9, 12, 18 and 24 months after surgery. The results showed that patients treated with either ACI or BMSCs had a significant improvement in their quality of life, however, men's health and sport activity showed a greater improvement than that of women. In the ACI group patients older than 45 years had less significant improvements than younger patients but this was not observed in the BMSC group. This study suggests that both treatments are an effective way of relieving pain and improving the quality of life. The advantages of BMCS treatment are that it requires one fewer surgeries and that the surgery is less invasive resulting in lower morbidity and hospitalization costs. Moreover, treatment with BMSCs showed no difference between age groups.

Bone-marrow derived MSCs in clinical use

The first report of using BMSCs to treat osteoarthritis was documented by Wakitani et al. in 2002[59]. The study consisted of 24 patients with knee osteoarthritis who underwent a high tibial osteotomy. Twelve of these patients received autologous BMSC transplantations and the other 12 served as a control group. BMSCs were harvested from the iliac crest and expanded in cultures. During the high tibial osteotomy, the knee joint was opened using the parapatellar medial approach. They observed the medial femoral condyle and medial tibial plateau; in all cases the articular cartilage on the medial femoral condyle was lost as well as the sub-condral bone being eburnated. The mean number of 1.3 x 10^7 BMSCs was introduced in a gel-cell composite consisting of 2 ml of 0.25% type I acid soluble collagen from the porcine tendon put onto a collagen sheet and gelatin. This gel-cell composite was applied to the abraded area and covered with collagen sheets. They were able to obtain samples of repair tissue and observe the transplants through arthroscopy in the following two surgeries when the pins and staples were removed. Clinical evaluations before and after surgeries were performed using the Hospital for Special Surgery knee-rating scale. Both groups showed significant improvements in pain, function and muscle strength. However, no difference was observed between the cell-transplanted group and cell-free group. Interestingly, it was observed that, the defects were covered with white soft tissue and some hyaline cartilage-like tissue in the cell-transplanted group. This was not the case for the cell-free group where white material with an irregular surface could be evident and in some areas underlying bone was visible. Although patients showed no improvement in the quality of life in either group, BMSCs seemed to be able to produce cartilage-like tissue in *in vivo* transplants.

Similar results were reported in 2007 by Kuroda et al. in a 31-year-old patient suffering from pain in the right knee[65]. BMSCs expanded in culture were introduced in a gel-cell composite through surgery. Seven months later arthroscopy revealed the defects to be covered with smooth tissue. Histological staining of samples showed hyaline-like type cartilage tissue that stained positively with Safranin-O. Twelve months after surgery magnetic resonance images (MRI) showed an increased thickness of the cartilage and that the bone was no longer edematous. The patient retained his previous activity level experiencing no pain or complications. These findings suggest that a transplant of autologous BMSCs can promote the repair of large focal articular cartilage defects. However, these studies showed promising results in cartilage repair by introducing cells through a major surgical operation. Since then, less invasive procedures have been suggested and performed by injecting BMSCs or AMSCs directly into the synovium of the knee joint or by preforming subchondral microdrilling combined with an injection of growth factors or substances such as hyaluronic acid which has been proved as being beneficial for cartilage health and repair[66,67].

In 2011, Saw et al. investigated the quality of articular cartilage regeneration after arthroscopic subchondral drilling[68]. They postoperatively injected five patients with autologous peripheral blood progenitor cells (PBPCs) in combination with hyaluronic acid (HA) for improving the regeneration of cartilage. The patients received the first injection one week after the surgery followed by four more injections at weekly intervals. They performed a second-look arthroscopy which confirmed articular cartilage regeneration and histologic sections stained positive suggesting the formation of hyaline cartilage, both of which are consistent results with previous findings. In addition, they also performed histologic and MRI studies of articular cartilage regeneration in patients treated with or without PBPCs and HA after arthroscopic subchondral drilling[69]. The intervention group's histologic scores and MRI scores were significantly better than those of the control group. It was concluded that treatment by regularly injecting PBSCs and HA after surgery improved the quality of articular cartilage repair. Studies on the effects of direct injection of MSCs without any surgical procedures have also shown promising results in the treatment of knee osteoarthritis (Fig. 1).

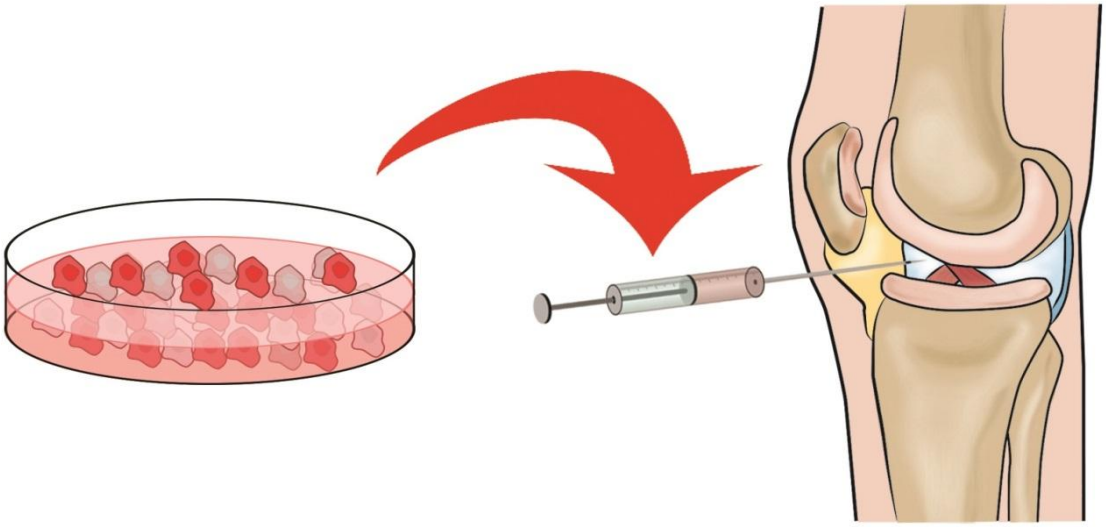


Fig. 1 Direct intra-articular injection of mesenchymal stem cells. Mesenchymal stem cells are harvested from various sites, most commonly bone-marrow or adipose tissues. They can be expanded in culture and then injected in suspension directly into the patients' knee.

Bone-marrow derived MSCs in the treatment of osteoarthritis

In 2011, Davatchi et al. reported their results on the direct injection of BMSCs into the knees of patients suffering from osteoarthritis[70]. All four patients in this study were over 50 years old and suffering from moderate to severe knee osteoarthritis due to obesity. BMSCs were obtained from 30 ml of bone-marrow blood from the patients and expanded in culture; they were confirmed as MSCs by immunophenotyping. The mean volume of 5.5 ml containing 8-9 x 10^6 cells was injected into one knee of each patient. Although improvement was observed in 3 out of 4 patient it was minor and the researcher concluded the results as encouraging, but not excellent. Another similar report from 2012 describes 6 female volunteers who needed total joint replacement (TJR) surgery but received a BMSCs injection instead[71]. In this study the obtained 50 ml of bone-marrow blood and expanded in culture, likewise they confirmed their cell population as MSCs by immunophenotyping. They injected 20-24 x 10^6 BMSCs intra-articularly into the knees of the volunteers. MRI demonstrated an increased cartilage thickness in 3 out of 6 patients and patients reported a reduction of pain as well as improvement in walking distance for the first 6 months then slightly reducing for the following 6 months. Taken together, these studies were both promising and encouraging but not fully satisfactory as a standard treatment for knee osteoarthritis.

More promising results with intra-articular injections of autologous BMSCs alone were produced in 2013 by Orozco et al.[72]. Their study consisted of 12 patients with osteoarthritic knee pain who failed conservative treatment and 9 out of 12 had already undergone previous surgery. Bone-marrow was extracted from the iliac crest for MSC isolation. Cells were expanded in culture and confirmed as MSCs by immunophenotyping. After 3 weeks of cell culture, cells were harvested and injected into the patients. The patients received an 8 ml of 40 x 10^6 cells injection which was considerably larger number than in previous comparable studies[70,71]. Clinical outcomes were followed for one year by evaluating pain, disability, quality of life as well as measuring articular cartilage quality through MRI. By 3 months, pain was significantly reduced with additional progress in the 9 months to follow and was significant at all-time points observed. Patients showed rapid and progressive improvement of the Lequesne index that approached 65-78% after 1 year. Patients were also satisfied with the treatment and 11 out of 12 reported lasting pain relief throughout the study period. MRI also showed a significant increase and improvement in cartilage quantity and quality in 11 out of 12 patients. Furthermore, it was demonstrated that the feasibility and safety of the treatment reached up to 78% of treatment results with 100% being a perfect treatment. It compared favorably with the conventional treatments producing considerably better results. Additionally, it compares well with other invasive methods such as TJR surgery since it is simple and does not require hospitalization or surgery, resulting in overall lower costs. Their results were considerably better than in the similar studies mentioned previously. One of the reasons might be that they injected approximately 2-4 times more MSCs than in the other two studies.

Adipose derived MSCs (AMSCs) as treatment for osteoarthritis

Although the main focus has been on the use of BMSCs, some researchers have chosen to use AMSCs as an alternative tissue. This is due to the abundance of available adipose tissue for cell harvesting and the higher yield obtained from each gram of tissue. In 2012 and 2013, Koh et al. published two papers on the same study which revolved around the use of AMSCs for the treatment of osteoarthritis[73, 74]. This study recruited 18 patients who received an injection of AMSCs to the knee. The adipose tissue was harvested from the inner side of the infrapatellar fat pad via a skin incision after arthroscopic debridement. Interestingly, they did not culture the cells but directly isolated them from the fat tissue by centrifuging the tissue sample. They did not perform immunophenotyping to confirm their cell population as MSCs, but simply counted them with a hemocytometer and presumed their cell population consisted of MSCs. Since this was a quick process, they were able to inject the cells back into the patients on the same day as they were harvested. They did not receive the same yield of cells from each patient and the injected cells ranged from 0.3×10^6 to 2.7×10^6 in number. Clinical outcomes were evaluated before treatment and in the following two years after treatment. Overall, the treatment was a success and there was no major complication. The data showed a significant reduction of pain and an increased quality of life for all patients. A positive correlation was found between the number of cells injected and pain improvement. Furthermore, MRI images taken before and after treatment confirmed that the whole-organ MRI score had increased significantly and the improvement was also correlated with the number of cells injected. They concluded that AMSCs were a valid cell source for treating cartilage damage. Their method is also simple and cost effective with cells being harvested and re-injected into the patient on the same day resulting in reduced costs from cell expansion and from the fact that no hospitalization is required. The weakness of their study was that they did not confirm their population as MSCs. Therefore, the cell population might consist of more cell types such as adipocytes. They also noted that the number of AMSCs that can be isolated for the infrapatellar fat pad is limited and a source that could provide a higher yield of stem cells would be preferable. The fact that they observed greater improvements in patients who received higher numbers of cells in their injections is consistent with the studies previously mentioned. Davatchi et al. injected 8-9 x 10^6 cells observing minimal improvement, Emadedin et al. injected 20-24 x 10^6 with promising results but not satisfactory while Orozco et al. injected 40 x 10^6 cells producing satisfactory and good results both in the quality of life for patients and articular cartilage regeneration[70-72]. The effectiveness of intra-articular delivery of MSCs in the knee has already been investigated in a number of clinical trials (Table 1).

Current clinical trials

Currently, a number of clinical trials are underway in the treatment of cartilage damage with MSCs. Out of the 13 clinical trials listed in the National Library of Medicine on the clinicaltrials.gov website in 2012, 11 are focused on the treatment of knee osteoarthritis[45]. They mainly revolve around the use of expanded autologous MSCs derived either from bone-marrow or adipose tissue, although some trials use allogenic or non-culture expanded MSCs. Most researchers focus on the use of intra-articular injections without the use of scaffolds or major surgeries since injections are more cost effective, cause little morbidity and are a desirable way of treatment if they are successful. Since optimal dose-studies have not been carried out yet the ideal dose of MSCs is unknown and doses in the current trials ranges from 1×10^7 to 1×10^8. These studies will further help in determining what tissues are good sources of viable MSCs for cartilage repair, what the optimal dose-size should be as well as demonstrating if a single injection is sufficient or multiple injections might be required for satisfying results.

Conclusion

The promising results from the studies described in this review show that there are alternative ways to treat moderate to late stage OA. The traditional major surgeries used to treat the condition are both expensive and come with risks. The less invasive methods described here have shown good results but the development of the treatment is ongoing. Better results were obtained with higher numbers of MSCs injected but the optimum dose still remains to be decided. Interestingly, no studies used multiple injections but instead all focused on a single injection hoping it would provide permanent relief of the condition. The results from the single injection studies showed that there was an improvement, but in some cases that improvement was reduced over time. Multiple or even regular injections of MSCs into the joints might be necessary. The dream solution would be a single injection of MSCs alone or in combination of growth factors, which would fully regenerate articular cartilage damage and result in a lasting tissue and eliminating the pain which follows the condition. In order to achieve such a dream solution, a number of studies are needed with satisfying and consistent results as well as determining all factors of the treatment such as dose-size, vehicles used to deliver and if any external factors are needed.

Table 1 Summary of studies where MSCs were used for treating articular cartilage damage in the knee joints

Study	Number of patients	Delivery system	Number of cells	Follow-up time	Control group	MSCs cell origin	Defects
Safety of autologous bone marrow-derived mesenchymal stem cell transplantation for cartilage repair in 41 patients with 45 joints followed for up to 11 years and 5 months[58]	41	Surgery, implantation, cell sheets, gel-cell composite	N/A	5-137 months	None	Autologous BMSCs from iliac crest	Various cartilage defects (not including osteoarthritis)
Autologous bone marrow derived mesenchymal stem cells versus autologous chondrocyte implantation[56]	36	ACI surgery, implantation cell sheets	1.0×10^7 – 1.5×10^7	24 months	36 patients receiving chondrocyte treatment	Autologous BMSCs from iliac crest	Knee cartilage defects (not including osteoarthritis)
Increased knee cartilage volume in degenerative joint disease using percutaneously implanted, autologous mesenchymal stem cells[75]	1	Three Intra-articular injection	2.24×10^7	3 months	None	Autologous BMSCs from iliac crest	Knee osteoarthritis
Osteochondral lesions of the knee: A new one-step repair technique with bone marrow-derived cells[76]	20	Surgery , implantation hyaluronic acid membrane scaffold	N/A, 2 ml of bone-marrow concentrate	24 months	None	Autologous BMSCs from iliac crest	Knee cartilage defects (including osteoarthritis)
Regeneration of meniscus cartilage in a knee treated with percutaneously implanted autologous mesenchymal stem cells[77]	1	Three timely spaced intra-articular injections	4.56×10^7	3 months	None	Autologous BMSCs from posterior superior iliac spine	Knee osteoarthritis
Treatment of a full-thickness articular cartilage defect in the femoral condyle of an athlete with autologous bone marrow stromal cells[65]	1	Surgery , implantation, gel –cell composite	N/A	12 months	None	Autologous BMSCs from iliac crest	Knee cartilage defect
Mesenchymal stem cell injections improve symptoms of knee osteoarthritis[74]	18	Single intra-articular injection	1.18×10^6	24 months	None	Autologous AMSCs from infrapatellar fat pad	Knee osteoarthritis
Infrapatellar fat pad-derived mesenchymal stem cell therapy for knee osteoarthritis[73]	25	Single intra-articular injection	1.18×10^6	12 months	25 cell free controls	Autologous AMSCs from infrapatellar fat pad	Knee osteoarthritis
Human autologous culture expanded bone marrow mesenchymal cell transplantation for repair of cartilage defects in osteoarthritic knees[59]	12	Surgery, implantation, cell sheets, gel –cell composite	1.3×10^7	28-95 weeks	12 cell free controls	Autologous BMSCs from iliac crest	Knee osteoarthritis
Intra-articular injection of autologous mesenchymal stem cells in six patients with knee osteoarthritis[71]	6	Single intra-articular injection	2.0×10^7 – 2.4×10^7	12 months	None	Autologous BMSCs from iliac crest	Knee osteoarthritis
Mesenchymal stem cell therapy for knee osteoarthritis. Preliminary report of four patients[70]	4	Single intra-articular injection	8.0×10^6 – 9.0×10^6	12 months	None	Autologous BMSCs	Knee osteoarthritis
Treatment of knee osteoarthritis with autologous mesenchymal stem cells: A pilot study[72]	12	Single intra-articular injection	4.0×10^7	12 months	None	Autologous BMSCs from iliac crest	Knee osteoarthritis

References

1. Buckwalter JA, Martin JA. Osteoarthritis. Adv Drug Deliv Rev 2006; 58: 150-67.
2. Davatachi F. Rheumatic diseases in the APLAR region. APLAR Journal of Rheumatology 2006; 9: 6.
3. Findlay DM. If good things come from above, do bad things come from below? Arthritis Res Ther 2010; 12: 119.
4. Goldring MB, Goldring SR. Articular cartilage and subchondral bone in the pathogenesis of osteoarthritis. Ann N Y Acad Sci 2010; 1192: 230-7.
5. de Lange-Brokaar BJ, Ioan-Facsinay A, van Osch GJ, Zuurmond AM, Schoones J, Toes RE, et al. Synovial inflammation, immune cells and their cytokines in osteoarthritis: a review. Osteoarthritis Cartilage 2012; 20: 1484-99.
6. Haq SA, Davatchi F, Dahaghin S, Islam N, Ghose A, Darmawan J, et al. Development of a questionnaire for identification of the risk factors for osteoarthritis of the knees in developing countries. A pilot study in Iran and Bangladesh. An ILAR-COPCORD phase III study. Int J Rheum Dis 2010; 13: 203-14.
7. Dahaghin S, Tehrani-Banihashemi SA, Faezi ST, Jamshidi AR, Davatchi F. Squatting, sitting on the floor, or cycling: are life-long daily activities risk factors for clinical knee osteoarthritis? Stage III results of a community-based study. Arthritis Rheum 2009; 61: 1337-42.
8. Gore M, Tai KS, Sadosky A, Leslie D, Stacey BR. Clinical comorbidities, treatment patterns, and direct medical costs of patients with osteoarthritis in usual care: a retrospective claims database analysis. J Med Econ 2011; 14: 497-507.
9. Le Pen C, Reygrobellet C, Gerentes I. Financial cost of osteoarthritis in France. The "COART" France study. Joint Bone Spine 2005; 72: 567-70.
10. Hermans J, Koopmanschap MA, Bierma-Zeinstra SM, van Linge JH, Verhaar JA, Reijman M, et al. Productivity costs and medical costs among working patients with knee osteoarthritis. Arthritis Care Res (Hoboken) 2012; 64: 853-61.
11. Hawker GA, Mian S, Bednis K, Stanaitis I. Osteoarthritis year 2010 in review: non-pharmacologic therapy. Osteoarthritis Cartilage 2011; 19: 366-74.
12. Pisters MF, Veenhof C, Schellevis FG, De Bakker DH, Dekker J. Long-term effectiveness of exercise therapy in patients with osteoarthritis of the hip or knee: a randomized controlled trial comparing two different physical therapy interventions. Osteoarthritis Cartilage 2010; 18: 1019-26.
13. Buckwalter JA, Saltzman C, Brown T. The impact of osteoarthritis: implications for research. Clin Orthop Relat Res 2004; 427S: S6-15.
14. Vasiliadis HS, Wasiak J. Autologous chondrocyte implantation for full thickness articular cartilage defects of the knee. Cochrane Database Syst Rev 2010; 10: CD003323.
15. Brittberg M, Lindahl A, Nilsson A, Ohlsson C, Isaksson O, Peterson L. Treatment of deep cartilage defects in the knee with autologous chondrocyte transplantation. N Engl J Med 1994; 331: 889-95.
16. Kurtz S, Ong K, Lau E, Mowat F, Halpern M. Projections of primary and revision hip and knee arthroplasty in the United States from 2005 to 2030. J Bone Joint Surg Am 2007; 89: 780-5.
17. Pittenger MF, Mackay AM, Beck SC, Jaiswal RK, Douglas R, Mosca JD, et al. Multilineage potential of adult human mesenchymal stem cells. Science 1999; 284: 143-7.
18. Gupta PK, Das AK, Chullikana A, Majumdar AS. Mesenchymal stem cells for cartilage repair in osteoarthritis. Stem Cell Res Ther 2012; 3: 25.
19. Yoo JU, Barthel TS, Nishimura K, Solchaga L, Caplan AI, Goldberg VM, et al. The chondrogenic potential of human bone-marrow-derived mesenchymal progenitor cells. J Bone Joint Surg Am 1998; 80: 1745-57.
20. Friedenstein AJ, Piatetzky S, II, Petrakova KV. Osteogenesis in transplants of bone marrow cells. J Embryol Exp Morphol 1966; 16: 381-90.
21. Dominici M, Le Blanc K, Mueller I, Slaper-Cortenbach I, Marini F, Krause D, et al. Minimal criteria for defining multipotent mesenchymal stromal cells. The International Society for Cellular Therapy position statement. Cytotherapy 2006; 8: 315-7.
22. Petersen BE, Bowen WC, Patrene KD, Mars WM, Sullivan AK, Murase N, et al. Bone marrow as a potential source of hepatic oval cells. Science 1999; 284: 1168-70.
23. Kopen GC, Prockop DJ, Phinney DG. Marrow stromal cells migrate throughout forebrain and cerebellum, and they differentiate into astrocytes after injection into neonatal mouse brains. Proc Natl Acad Sci U S A 1999; 96: 10711-6.
24. Ma K, Laco F, Ramakrishna S, Liao S, Chan CK. Differentiation of bone marrow-derived mesenchymal stem cells into multi-layered epidermis-like cells in 3D organotypic coculture. Biomaterials 2009; 30: 3251-8.
25. Dai LJ, Li HY, Guan LX, Ritchie G, Zhou JX. The therapeutic potential of bone marrow-derived mesenchymal stem cells on hepatic cirrhosis. Stem Cell Res 2009; 2: 16-25.
26. Campagnoli C, Roberts IA, Kumar S, Bennett PR, Bellantuono I, Fisk NM. Identification of

mesenchymal stem/progenitor cells in human first-trimester fetal blood, liver, and bone marrow. Blood 2001; 98: 2396-402.
27. Karp JM, Leng Teo GS. Mesenchymal stem cell homing: the devil is in the details. Cell Stem Cell 2009; 4: 206-16.
28. Uccelli A, Moretta L, Pistoia V. Mesenchymal stem cells in health and disease. Nat Rev Immunol 2008; 8: 726-36.
29. Doorn J, Moll G, Le Blanc K, van Blitterswijk C, de Boer J. Therapeutic applications of mesenchymal stromal cells: paracrine effects and potential improvements. Tissue Eng Part B Rev 2012; 18: 101-15.
30. Meirelles Lda S, Fontes AM, Covas DT, Caplan AI. Mechanisms involved in the therapeutic properties of mesenchymal stem cells. Cytokine Growth Factor Rev 2009; 20: 419-27.
31. Salgado AJ, Reis RL, Sousa NJ, Gimble JM. Adipose tissue derived stem cells secretome: soluble factors and their roles in regenerative medicine. Curr Stem Cell Res Ther 2010; 5: 103-10.
32. Bunnell BA, Estes BT, Guilak F, Gimble JM. Differentiation of adipose stem cells. Methods Mol Biol 2008; 456: 155-71.
33. Crisan M, Yap S, Casteilla L, Chen CW, Corselli M, Park TS, et al. A perivascular origin for mesenchymal stem cells in multiple human organs. Cell Stem Cell 2008; 3(3): 301-13.
34. Troyer DL, Weiss ML. Wharton's jelly-derived cells are a primitive stromal cell population. Stem Cells 2008; 26: 591-9.
35. Sacchetti B, Funari A, Michienzi S, Di Cesare S, Piersanti S, Saggio I, et al. Self-renewing osteoprogenitors in bone marrow sinusoids can organize a hematopoietic microenvironment. Cell 2007; 131: 324-36.
36. Bernardo ME, Zaffaroni N, Novara F, Cometa AM, Avanzini MA, Moretta A, et al. Human bone marrow derived mesenchymal stem cells do not undergo transformation after long-term in vitro culture and do not exhibit telomere maintenance mechanisms. Cancer Res 2007; 67: 9142-9.
37. Suzuki K, Sun R, Origuchi M, Kanehira M, Takahata T, Itoh J, et al. Mesenchymal stromal cells promote tumor growth through the enhancement of neovascularization. Mol Med 2011; 17: 579-87.
38. De Bari C, Dell'Accio F, Tylzanowski P, Luyten FP. Multipotent mesenchymal stem cells from adult human synovial membrane. Arthritis Rheum 2001; 44: 1928-42.
39. Segawa Y, Muneta T, Makino H, Nimura A, Mochizuki T, Ju YJ, et al. Mesenchymal stem cells derived from synovium, meniscus, anterior cruciate ligament, and articular chondrocytes share similar gene expression profiles. J Orthop Res 2009; 27: 435-41.
40. Steinert AF, Kunz M, Prager P, Barthel T, Jakob F, Noth U, et al. Mesenchymal stem cell characteristics of human anterior cruciate ligament outgrowth cells. Tissue Eng Part A 2011; 17: 1375-88.
41. Khan WS, Adesida AB, Tew SR, Longo UG, Hardingham TE. Fat pad-derived mesenchymal stem cells as a potential source for cell-based adipose tissue repair strategies. Cell Prolif 2012; 45: 111-20.
42. Williams R, Khan IM, Richardson K, Nelson L, McCarthy HE, Analbelsi T, et al. Identification and clonal characterisation of a progenitor cell sub-population in normal human articular cartilage. PLoS One 2010; 5: e13246.
43. Barry FP, Murphy JM. Mesenchymal stem cells: clinical applications and biological characterization. Int J Biochem Cell Biol 2004; 36: 568-84.
44. Karystinou A, Dell'Accio F, Kurth TB, Wackerhage H, Khan IM, Archer CW, et al. Distinct mesenchymal progenitor cell subsets in the adult human synovium. Rheumatology (Oxford) 2009; 48: 1057-64.
45. Barry F, Murphy M. Mesenchymal stem cells in joint disease and repair. Nat Rev Rheumatol 2013;9:584-94.
46. Flannery CR, Hughes CE, Schumacher BL, Tudor D, Aydelotte MB, Kuettner KE, et al. Articular cartilage superficial zone protein (SZP) is homologous to megakaryocyte stimulating factor precursor and Is a multifunctional proteoglycan with potential growth-promoting, cytoprotective, and lubricating properties in cartilage metabolism. Biochem Biophys Res Commun 1999; 254: 535-41.
47. Lee DH, Sonn CH, Han SB, Oh Y, Lee KM, Lee SH. Synovial fluid CD34(-) CD44(+) CD90(+) mesenchymal stem cell levels are associated with the severity of primary knee osteoarthritis. Osteoarthritis Cartilage 2012; 20: 106-9.
48. Murphy JM, Dixon K, Beck S, Fabian D, Feldman A, Barry F. Reduced chondrogenic and adipogenic activity of mesenchymal stem cells from patients with advanced osteoarthritis. Arthritis Rheum 2002; 46: 704-13.
49. Scharstuhl A, Schewe B, Benz K, Gaissmaier C, Buhring HJ, Stoop R. Chondrogenic potential of human adult mesenchymal stem cells is independent of age or osteoarthritis etiology. Stem Cells 2007; 25: 3244-51.
50. Wakitani S, Kimura T, Hirooka A, Ochi T, Yoneda M, Yasui N, et al. Repair of rabbit articular surfaces with allograft chondrocytes embedded in collagen gel. J Bone Joint Surg Br 1989; 71: 74-80.
51. Ochi M, Uchio Y, Kawasaki K, Wakitani S, Iwasa J. Transplantation of cartilage-like tissue

made by tissue engineering in the treatment of cartilage defects of the knee. J Bone Joint Surg Br 2002; 84: 571-8.
52. Wakitani S, Goto T, Pineda SJ, Young RG, Mansour JM, Caplan AI, et al. Mesenchymal cell-based repair of large, full-thickness defects of articular cartilage. J Bone Joint Surg Am 1994; 76: 579-92.
53. Aust L, Devlin B, Foster SJ, Halvorsen YD, Hicok K, du Laney T, et al. Yield of human adipose-derived adult stem cells from liposuction aspirates. Cytotherapy 2004; 6: 7-14.
54. Pei M, He F, Boyce BM, Kish VL. Repair of full-thickness femoral condyle cartilage defects using allogeneic synovial cell-engineered tissue constructs. Osteoarthritis Cartilage 2009; 17: 714-22.
55. Shirasawa S, Sekiya I, Sakaguchi Y, Yagishita K, Ichinose S, Muneta T. In vitro chondrogenesis of human synovium-derived mesenchymal stem cells: optimal condition and comparison with bone marrow-derived cells. J Cell Biochem 2006; 97: 84-97.
56. Nejadnik H, Hui JH, Feng Choong EP, Tai BC, Lee EH. Autologous bone marrow-derived mesenchymal stem cells versus autologous chondrocyte implantation: an observational cohort study. Am J Sports Med 2010; 38: 1110-6.
57. Wakitani S, Mitsuoka T, Nakamura N, Toritsuka Y, Nakamura Y, Horibe S. Autologous bone marrow stromal cell transplantation for repair of full-thickness articular cartilage defects in human patellae: two case reports. Cell Transplant 2004; 13: 595-600.
58. Wakitani S, Okabe T, Horibe S, Mitsuoka T, Saito M, Koyama T, et al. Safety of autologous bone marrow-derived mesenchymal stem cell transplantation for cartilage repair in 41 patients with 45 joints followed for up to 11 years and 5 months. J Tissue Eng Regen Med 2011; 5: 146-50.
59. Wakitani S, Imoto K, Yamamoto T, Saito M, Murata N, Yoneda M. Human autologous culture expanded bone marrow mesenchymal cell transplantation for repair of cartilage defects in osteoarthritic knees. Osteoarthritis Cartilage 2002; 10: 199-206.
60. Karnoub AE, Dash AB, Vo AP, Sullivan A, Brooks MW, Bell GW, et al. Mesenchymal stem cells within tumour stroma promote breast cancer metastasis. Nature 2007; 449: 557-63.
61. Spaeth EL, Dembinski JL, Sasser AK, Watson K, Klopp A, Hall B, et al. Mesenchymal stem cell transition to tumor-associated fibroblasts contributes to fibrovascular network expansion and tumor progression. PLoS One 2009; 4: e4992.
62. Fu FH, Zurakowski D, Browne JE, Mandelbaum B, Erggelet C, Moseley JB, Jr., et al. Autologous chondrocyte implantation versus debridement for treatment of full-thickness chondral defects of the knee: an observational cohort study with 3-year follow-up. Am J Sports Med 2005; 33(11): 1658-66.
63. Vinatier C, Bouffi C, Merceron C, Gordeladze J, Brondello JM, Jorgensen C, et al. Cartilage tissue engineering: towards a biomaterial-assisted mesenchymal stem cell therapy. Curr Stem Cell Res Ther 2009; 4: 318-29.
64. Aung A, Gupta G, Majid G, Varghese S. Osteoarthritic chondrocyte-secreted morphogens induce chondrogenic differentiation of human mesenchymal stem cells. Arthritis Rheum 2011; 63: 148-58.
65. Kuroda R, Ishida K, Matsumoto T, Akisue T, Fujioka H, Mizuno K, et al. Treatment of a full-thickness articular cartilage defect in the femoral condyle of an athlete with autologous bone-marrow stromal cells. Osteoarthritis Cartilage 2007; 15: 226-31.
66. Kaplan LD, Lu Y, Snitzer J, Nemke B, Hao Z, Biro S, et al. The effect of early hyaluronic acid delivery on the development of an acute articular cartilage lesion in a sheep model. Am J Sports Med 2009; 37: 2323-7.
67. Turajane T, Chaweewannakorn U, Larbpaiboonpong V, Aojanepong J, Thitiset T, Honsawek S, et al. Combination of intra-articular autologous activated peripheral blood stem cells with growth factor addition/ preservation and hyaluronic acid in conjunction with arthroscopic microdrilling mesenchymal cell stimulation Improves quality of life and regenerates articular cartilage in early osteoarthritic knee disease. J Med Assoc Thai 2013; 96: 580-8.
68. Saw KY, Anz A, Merican S, Tay YG, Ragavanaidu K, Jee CS, et al. Articular cartilage regeneration with autologous peripheral blood progenitor cells and hyaluronic acid after arthroscopic subchondral drilling: a report of 5 cases with histology. Arthroscopy 2011; 27: 493-506.
69. Saw KY, Anz A, Siew-Yoke Jee C, Merican S, Ching-Soong Ng R, Roohi SA, et al. Articular cartilage regeneration with autologous peripheral blood stem cells versus hyaluronic acid: a randomized controlled trial. Arthroscopy 2013; 29: 684-94.
70. Davatchi F, Abdollahi BS, Mohyeddin M, Shahram F, Nikbin B. Mesenchymal stem cell therapy for knee osteoarthritis. Preliminary report of four patients. Int J Rheum Dis 2011; 14: 211-5.
71. Emadedin M, Aghdami N, Taghiyar L, Fazeli R, Moghadasali R, Jahangir S, et al. Intra-articular injection of autologous mesenchymal stem cells

in six patients with knee osteoarthritis. Arch Iran Med 2012; 15: 422-8.
72. Orozco L, Munar A, Soler R, Alberca M, Soler F, Huguet M, et al. Treatment of knee osteoarthritis with autologous mesenchymal stem cells: a pilot study. Transplantation 2013; 95: 1535-41.
73. Koh YG, Choi YJ. Infrapatellar fat pad-derived mesenchymal stem cell therapy for knee osteoarthritis. Knee 2012; 19: 902-7.
74. Koh YG, Jo SB, Kwon OR, Suh DS, Lee SW, Park SH, et al. Mesenchymal stem cell injections improve symptoms of knee osteoarthritis. Arthroscopy 2013; 29: 748-55.
75. Centeno CJ, Busse D, Kisiday J, Keohan C, Freeman M, Karli D. Increased knee cartilage volume in degenerative joint disease using percutaneously implanted, autologous mesenchymal stem cells. Pain Physician 2008; 11: 343-53.
76. Buda R, Vannini F, Cavallo M, Grigolo B, Cenacchi A, Giannini S. Osteochondral lesions of the knee: a new one-step repair technique with bone-marrow-derived cells. J Bone Joint Surg Am 2010; 92 S2: 2-11.
77. Centeno CJ, Busse D, Kisiday J, Keohan C, Freeman M, Karli D. Regeneration of meniscus cartilage in a knee treated with percutaneously implanted autologous mesenchymal stem cells. Med Hypotheses 2008; 71: 900-8.

เซลล์ต้นกำเนิดมีเซนไคมอลสำหรับการรักษารอยโรคกระดูกอ่อนในโรคข้อเสื่อม

บาลเดอร์ คริสเตียนสัน, โทมัส มาเบย, พงศ์ศักดิ์ ยุกตะนันทน์, พบ, วินัย พากเพียร, พบ, สิทธิศักดิ์ หรรษาเวก, พบ

โรคข้อเสื่อมเป็นโรคที่เกิดพยาธิสภาพภายในข้อ ทำให้มีการสูญเสียกระดูกอ่อนผิวข้อ และเป็นปัญหาที่สำคัญต่อสุขภาพโดยเฉพาะผู้สูงวัยซึ่งมีจำนวนประชากรเพิ่มขึ้น กระดูกอ่อนมีศักยภาพในการเจริญสร้างทดแทนใหม่ได้จำกัด ดังนั้นรอยโรคกระดูกอ่อนเกิดจากการเสื่อมสภาพของกระดูกอ่อนอย่างช้าทีละน้อย ทำให้ผู้ป่วยโรคข้อเสื่อมเกิดอาการเจ็บปวดและสูญเสียการใช้งานของข้อ การรักษารอยโรคกระดูกอ่อนส่วนใหญ่เป็นการรักษาเพื่อบรรเทาอาการเจ็บปวดและการรักษาโดยการผ่าตัด เพื่อเพิ่มคุณภาพชีวิตให้แก่ผู้ป่วย การศึกษาวิจัยโดยให้ความสำคัญและเข้าใจกลไกการเกิดพยาธิสภาพของโรคข้อเสื่อม มีส่วนช่วยในการพัฒนาวิธีการรักษาโรคข้อเสื่อมได้ดีขึ้น

ในปัจจุบันมีการศึกษาวิจัย โดยใช้เซลล์ต้นกำเนิดมีเซนไคมอลในการรักษาโรคข้อเสื่อมมากขึ้น การทดลองทางคลินิกทั้งในสัตว์ทดลองและในมนุษย์ที่ผ่านมา มีหลักฐานพบว่าการใช้เซลล์ต้นกำเนิดอาจเป็นการรักษาที่สามารถทำได้ง่ายและมีประสิทธิภาพในการรักษารอยโรคกระดูกอ่อนและโรคข้อเสื่อม ความคาดหวังดังกล่าวคงไม่ไกลเกินความจริง บทความปริทรรศน์นี้เป็นการสรุปรวบรวมการศึกษาวิจัยโดยการใช้เซลล์ต้นกำเนิดที่สำคัญในการรักษารอยโรคกระดูกอ่อนและโรคข้อเสื่อม

Instruction to authors

Aims and scope

The Thai Journal of Orthopaedic Surgery is an official journal of **The Royal College of Orthopaedic Surgeons of Thailand**. It will accept original papers on clinical and experimental research that are pertinent in Orthopaedics. Original articles, short communication, case reports, review articles, letters to the Editor and miscellany are welcome.

It publishes: *original papers* - reporting progress and results in all areas of orthopaedics and its related fields; *review articles* - reflecting the present state of knowledge in special areas of summarizing limited themes in which discussion has led to clearly defined conclusions; *educational articles* - giving information on the progress of a topic of particular interest; *case reports* - of uncommon or interesting presentations of the condition.

Submission information

Online Submission

We are pleased to announce that we have moved to the online system of manuscript tracking, Authors are encouraged to submit their articles to **secretariat@rcost.or.th** or **supawineep@rcost.or.th** This will allow even quicker and more efficient processing of your manuscript.

Article types

- Original articles: word limit 5000 words, 45 references, no more than 6 figures/tables
- Short communications: 2500 words, 20 references, no more than 2 figures/tables.
- Reviews: word limit 10000 words, 100 references, no more than 10 figures
- Case Reports: 1500 words, 1-2 figures/tables, 20 references
- Letters: 500 words
- Editorial

Manuscript preparation

- Authorship Criteria and Contributions

All listed authors should have seen and approved the final version of the manuscript.

All authors of accepted articles must sign an authorship form affirming that they have met all three of the following criteria for authorship, thereby accepting public responsibility for appropriate portions of the content:

1. substantial contributions to conception and design, or acquisition of data, or analysis and interpretation of data;
2. drafting the article or revising it critically for important intellectual content;
3. approval of the version to be published and all subsequent versions.

If authorship is attributed to a group (such as for multi-center trials), the group must designate one or more individuals as authors or members of a writing group who meet full authorship criteria and who accepts direct responsibility for the manuscript.

Other group members who are not authors should be listed in the Acknowledgment section of the manuscript as participating investigators.

Individuals who do not meet the criteria for authorship but who have made substantial, direct contributions to the work (e.g., purely technical help, writing assistance, general or financial or material support) should be acknowledged in the Acknowledgments section of the manuscript, with a brief description of their contributions. Authors should

obtain written permission from anyone they wish to list in the Acknowledgments section.

- Redundant, Duplicate or Fraudulent Publication

Authors must not simultaneously submit their manuscripts to another publication if that manuscript is under consideration by Osteoporosis International.

Redundant or duplicate publication is a paper that overlaps substantially with one already published in print or electronic media. At the time of manuscript submission, authors must inform the editor about all submissions and previous publications that might be regarded as redundant or duplicate publication of the same or very similar work. Any such publication must be referred to and referenced in the new paper.Copies of such material should be included with the submitted paper as a supplemental file.

Authors must not:

- Willfully and knowingly submit false data
- Submit data from source not the authors' own
- Submit previously published material (with the exception of abstracts) without correct and proper citation
- Omit reference to the works of other investigators which established a priority
- Falsely certify that the submitted work is original
- Use material previously published elsewhere without prior written approval of the copyright holder

Title Page

The title page must be written in both Thai and English and should include:

- The name(s) of the author(s)
- A concise and informative title
- The affiliation(s) and address(es) of the author(s)
- The e-mail address, telephone and fax numbers of the corresponding author

Abstract

Please provide a structured abstract in both Thai and English of 250 words which should be divided into the following sections:

- Purpose (stating the main purposes and research question)
- Methods
- Results
- Conclusions

Keywords

Please provide 4 to 6 keywords which can be used for indexing purposes.

The manuscript: The manuscript must be written in English or Thai.

Text Formatting

The text should be organized in the following order: Introduction, Methods, Results, Discussion, Acknowledgements, References, Tables and Figures. Manuscripts should be submitted in Word.

- Use a normal, plain font (e.g., 10-point Times Roman) for text.
- Use italics for emphasis.
- Use the automatic page numbering function to number the pages.

- Do not use field functions.
- Use tab stops or other commands for indents, not the space bar.
- Use the table function, not spreadsheets, to make tables.
- Use the equation editor or MathType for equations.
- Note: If you use Word 2007, do not create the equations with the default equation editor but use the Microsoft equation editor or MathType instead.
- Save your file in doc format. Do not submit docx files.

Headings

Please use no more than three levels of displayed headings.

Abbreviations

Abbreviations should be defined at first mention and used consistently thereafter.

Footnotes

Footnotes on the title page are not given reference symbols. Footnotes to the text are numbered consecutively; those to tables should be indicated by superscript lower-case letters (or asterisks for significance values and other statistical data).

Acknowledgements

Acknowledgements of people, grants, funds, etc. should be placed in a separate section before the reference list. The names of funding organizations should be written in full.

Tables

- All tables are to be numbered using Arabic numerals.
- Tables should always be cited in text in consecutive numerical order.
- For each table, please supply a table heading. The table title should explain clearly and concisely the components of the table.
- Identify any previously published material by giving the original source in the form of a reference at the end of the table heading.
- Footnotes to tables should be indicated by superscript lower-case letters (or asterisks for significance values and other statistical data) and included beneath the table body.

Figures

Electronic Figure Submission

- Supply all figures electronically.
- Indicate what graphics program was used to create the artwork.
- For vector graphics, the preferred format is EPS; for halftones, please use TIFF format. MS Office files are also acceptable.
- Vector graphics containing fonts must have the fonts embedded in the files.
- Name your figure files with "Fig" and the figure number, e.g., Fig1.eps.

References: List the references in consecutive, numerical order, as they are cited in the text. Use the Vancouver style. If the list of authors exceeds 6, the first 6 authors followed by et al should be listed for those references. Abbreviate journal titles according to the style used in the Index Medicus. See also http://www.medscape.com/home/search/indexMedicus/ Index Medicus-A.html

Example of references:

Journal articles.

1. You CH, Lee KY, Chey RY, Menguy R. Electrogastrographic study of patient with unexplained nausea, bloating and vomiting. Gastroenterol 1980;79:311-4.
2. Gulgolgarn V, Ketsararat V, Niyomthai R, et al. Somatic growth and clinical manifestation in formula fed infants born to HIV-infected mothers during the first year of life. J Med Assoc Thai 1999;82:1094-9.

Conference proceeding

1. Bengtsson S, Solheim BG. Enforcement of data protection, privacy and security in medical informatics. In: Lun KC, Degoulet P, Peimme TE, Reinhoff O, editors. MEDINFO 92. Proceeding fo the 7th World Congress on Medical informatics; 1992 Sep 6-10; Geneva, Switzerland. Amsterdam: North-Holland; 1992. p.1561-5.

Abstract in scientific presentation

1. Wettstein A, Dore G, Murphy C, Hing M, Edward P. HIV-related cholangiopathy in Australia. IX Annual Conference of the Australasian Society of HIV Medicine. Adelaide, November 1997 [abstract P45].
2. Clement J, De Bock R. Hematological complications of hantavirus nephropathy [abstract]. Kidney Int 1992;42:1285.

Book

1. Getzen TE. Health economics: Fundamentals of funds. New York: John Wiley & Sons; 1997.
2. Porter RJ, Meldrum BS. Antiepileptic drugs. In: Katzung BG, editor. Basic and clinical pharmacology. 6th ed. Norwalk: Appleton & Lange; 1995. p.361-80.

Electronic article

1. Morse SS. Factors in the emergence of infectious disease. Emerg Infect Dis [serial online] 1995 Jan-Mar;1(1):[24 screens]. Available from: URL:http://www/cdc/gov/ncidoc/EID/eid.htm. Accessed December 25,1999.
2. LaPorte RE, Marler E, Akazawa S, Sauer F. The death of biomedical journals. BMJ [serial online]. 1995;310:1387-90. Available from: http://www.bmj.com/bmj/archive/6991ed2.htm. Accessed September 26,1996.
3. Health on the net foundation. Health on the net foundation code of conduct (HONcode) for medical and health web sites. Available at: http://www.hon.ch/Conduct.html. Accessed June 30, 1998.

คำแนะนำสำหรับผู้ส่งบทความเพื่อลงตีพิมพ์

จุดมุ่งหมายและขอบเขต

วารสาร The Thai Journal of Orthopaedic Surgery เป็นวารสารทางวิชาการของราชวิทยาลัยแพทย์ออร์โธปิดิกส์แห่งประเทศไทยที่พิมพ์เผยแพร่อย่างสม่ำเสมอทุก 3 เดือน (4 ฉบับ/ปี) ทั้งแบบเป็นเอกสารรูปเล่ม และแบบออนไลน์ โดยเป็นวารสารที่ได้รับการประเมินบทความโดยผู้ทรงคุณวุฒิ (peer–reviewed journal) เพื่อเปิดโอกาสให้นักวิชาการที่สนใจเสนอบทความที่เกี่ยวข้องกับการรักษาผู้ป่วยและผลงานวิจัยทางศัลยศาสตร์ออร์โธปิดิกส์

เพื่อรักษามาตรฐานของวารสาร บทความที่จะลงตีพิมพ์ในวารสารจำเป็นต้องเขียนเป็นภาษาอังกฤษ ซึ่งประกอบด้วย Original Articles, Case Report, Review Articles, Letter to the Editor และ Miscellany

บทความประเภท Original articles เป็นรายงานผลการวิจัยทางด้านศัลยศาสตร์ออร์โธปิดิกส์ และสาขาอื่นที่เกี่ยวข้อง

บทความ Review articles เป็นบทความที่รวบรวมเอาผลงานในเรื่องใดเรื่องหนึ่งโดยเฉพาะ ซึ่งเคยลงตีพิมพ์มาแล้ว นำมาวิเคราะห์ วิจารณ์ เพื่อให้เกิดความกระจ่างในเรื่องนั้นยิ่งขึ้น

รายงานผู้ป่วย (Case report) เป็นรายงานผู้ป่วย วิจารณ์อาการทางคลินิกและผลตรวจทางห้องปฏิบัติการที่น่าสนใจ

เรื่องที่ส่งมาต้องไม่เคยพิมพ์เผยแพร่มาก่อน กองบรรณาธิการขอสงวนสิทธิ์ในการตรวจทาน แก้ไขต้นฉบับ และพิจารณาตีพิมพ์ข้อคิดเห็นในบทความเป็นความเห็นและเป็นความรับผิดชอบของเจ้าของบทความโดยตรง

การส่งบทความ

ทางราชวิทยาลัยฯ ขอแจ้งให้ทราบว่า เพื่อความสะดวกรวดเร็วและมีประสิทธิภาพในการส่งบทความ ราชวิทยาลัยฯ ผู้เขียนสามารถเสนอบทความเพื่อพิจารณาได้ทางจดหมายอิเล็กโทรนิกส์ secretariat@rcost.or.th และ supawineep@rcost.or.th

ประเภทของบทความ

- นิพนธ์ต้นฉบับ (original articles) ให้มีความยาวไม่เกิน 5,000 คำ, เอกสารอ้างอิงไม่เกิน 40 ข้อ, รูปภาพและตารางรวมกันไม่เกิน 6 รูป
- บทความปริทรรศน์ (review articles) ให้มีความยาวไม่เกิน 10,000 คำ, เอกสารอ้างอิงไม่เกิน 100 ข้อ, รูปภาพและตารางรวมกันไม่เกิน 10 รูป
- รายงานผู้ป่วย (case report) ให้มีความยาวได้ 1,500 คำ, รูปภาพและตาราง 1–2 รูป/ตาราง, เอกสารอ้างอิงไม่เกิน 20 ข้อ
- จดหมายให้มีความยาวได้ 500 คำ
- บทบรรณาธิการ

การเตรียมต้นฉบับ

- **เกณฑ์การเขียนบทความ**

1. อธิบายเนื้อหาของบทความหรือวิเคราะห์ข้อมูลที่ได้มาให้ชัดเจน

2. หากต้นฉบับมีข้อผิดพลาดของรูปแบบหรือมีความไม่สมบูรณ์ขององค์ประกอบในบทความ บทความนั้นจะถูกส่งกลับไปยังผู้เขียนเพื่อทำการแก้ไขต่อไป
3. แก้ไขปรับปรุงเนื้อหาของต้นฉบับตามคำแนะนำของผู้ประเมินบทความ

หากมีการเขียนบทความโดยกลุ่ม กรุณาระบุชื่อผู้เขียนทุกคน และระบุชื่อผู้วิจัยหลักให้ชัดเจน

ควรแสดงความขอบคุณแก่บุคคลที่ไม่ได้มีส่วนร่วมในการเขียนบทความ แต่มีส่วนช่วยเหลือโดยตรงในการวิจัย เช่น ผู้ช่วยทางเทคนิค, ที่ปรึกษาด้านการเขียนบทความ, ผู้สนับสนุนทุนและวัสดุในการทำงานวิจัย เป็นต้น ไว้ในกิตติกรรมประกาศ (acknowledgements)

- **บทความที่ส่งมาจะต้องเป็นเรื่องที่ไม่เคยตีพิมพ์ที่ใดมาก่อน และผู้เขียนจะต้องไม่ส่งบทความเพื่อไปตีพิมพ์ในวารสารฉบับอื่นในเวลาเดียวกัน**

หลักเกณฑ์สำหรับผู้เขียนบทความ

- ผู้เขียนบทความต้องไม่มีเจตนาส่งข้อมูลเท็จ
- บทความที่ส่งมาต้องเป็นผลงานของท่านเอง
- ผู้เขียนบทความจะต้องไม่ส่งบทความที่เคยลงตีพิมพ์ในวารสารอื่น โดยไม่ระบุว่าท่านได้เสนอผลงานนั้นในวารสารใดบ้างอย่างถูกต้องและสมเหตุสมผล
- ต้องระบุรายชื่อผู้เขียนทุกคนตามความเป็นจริง
- ผู้เขียนบทความต้องส่งต้นฉบับที่ได้รับการรับรองที่แท้จริง
- ผู้เขียนบทความต้องไม่ใช้วิธีการศึกษาที่มีผู้เผยแพร่มาก่อน โดยไม่ได้รับการอนุมัติจากเจ้าของลิขสิทธิ์

- **หน้าแรก (Title page)** เขียนเป็นภาษาไทยและภาษาอังกฤษ ประกอบด้วย
  (1) ชื่อ สกุลของผู้เขียน
  (2) ชื่อเรื่องอย่างย่อ ที่สื่อความหมายและชี้ให้เห็นสาระสำคัญของเนื้อหาในตัวบทความ
  (3) สถานที่ทำงาน
  (4) เบอร์โทรศัพท์, เบอร์แฟกซ์ และe-mail address ของผู้เขียน
- **บทคัดย่อ (Abstract)** ต้องมีทั้งภาษาไทยและภาษาอังกฤษมีความยาวไม่เกิน 250 คำ โดยเรียงลำดับเนื้อหา ดังนี้
  (1) วัตถุประสงค์ (Purpose)
  (2) วิธีการศึกษา (Methods)
  (3) ผลการศึกษา (Results)
  (4) สรุป (Conclusions**)**
- **คำสำคัญ (Keyword)** ระบุไว้ใต้บทคัดย่อ มีความยาว 4 – 6 คำ
- **ต้นฉบับ (Manuscript)** เป็นภาษาอังกฤษ
- **เนื้อเรื่อง (Text Formatting)** ให้ลำดับความสำคัญของเนื้อหาดังนี้คือ บทนำ (introduction), วิธีการศึกษา (methods), ผลการศึกษา (results), วิจารณ์ (discussion), บทขอบคุณ (acknowledgements), เอกสารอ้างอิง (references), ตารางและรูปภาพประกอบ (tables and figures) โดยต้นฉบับจะต้องใช้รูปแบบ ดังนี้

(1) ใช้ตัวพิมพ์มาตรฐาน เช่นภาษาอังกฤษ ใช้ตัวอักษร “Times Roman” ขนาด 10 point ภาษาไทยใช้ ตัวอักษร “Angsana New” ขนาด 12 point

(2) พิมพ์ข้อความสำคัญด้วยตัวเอน

(3) ตั้งค่าเลขหน้าโดยอัตโนมัติ

(4) ไม่ใช้ “field functions”

(5) ใช้ปุ่ม “Tab” เมื่อขึ้นย่อหน้าต่อไป

(6) เลือกคำสั่งตาราง (Table) เมื่อต้องการพิมพ์ตาราง

(7) หากใช้โปรแกรม “Microsoft Word 2007” ให้ใช้โปรแกรม “Microsoft equation editor” หรือโปรแกรม “Math Type”

(8) ส่งต้นฉบับในรูปของแฟ้มข้อมูล โดยบันทึกข้อมูลเป็นไฟล์ “.doc” และห้ามบันทึกเป็นไฟล์ “.docx”

- **หัวข้อ (headings)** ไม่ควรมีขนาดต่างๆมากกว่า 3 ระดับ
- **คำย่อ (abbreviations)** จะต้องมีคำเต็มเมื่อปรากฏเป็นครั้งแรกในบทความ หลังจากนั้นสามารถใช้คำย่อเหล่านั้นได้ตามปกติ
- **เชิงอรรถ (footnotes)** คือ การอ้างอิงข้อความที่ผู้เขียนนำมากล่าวแยกจากเนื้อหาอยู่ตอนล่างของหน้า โดยใส่หมายเลขกำกับไว้ท้ายข้อความที่คัดลอกหรือเก็บแนวคิดมา และจะไม่เขียนเชิงอรรถเอาไว้ที่หน้าแรกของบทความ ถ้าต้องการแสดงที่มาของตารางหรือภาพประกอบให้ใช้เครื่องหมายแทนตัวเลข โดยเขียนไว้ที่ส่วนล่าง ของหน้า หรือใช้เครื่องหมายดอกจัน (*) เพื่อแสดงความหมายของค่าหรือข้อมูลทางสถิติ
- **กิตติกรรมประกาศ (acknowledgements)** เป็นการแสดงความขอบคุณแก่ผู้ที่ช่วยเหลือในการทำวิจัย หรือผู้สนับสนุนทุนการวิจัย เป็นต้น โดยจะเขียนไว้ก่อนเอกสารอ้างอิงและควรเขียนชื่อสถาบันที่ให้การสนับสนุนทุนการวิจัยโดยใช้ชื่อเต็ม
- **ตาราง (tables)**

(1) ให้เขียนหมายเลขตารางเป็นเลขอารบิก

(2) ให้เรียงตามลำดับที่ของตารางอย่างต่อเนื่องกันจาก 1, 2, 3, ….

(3) การอธิบายผลในตารางต้องไม่ซ้ำซ้อนกันและมีใจความกระชับรัดกุม และมีคำอธิบายกำกับไว้เหนือตาราง

(4) เขียนคำอธิบายเพิ่มเติมเกี่ยวกับแหล่งที่มาของเอกสารอ้างอิงไว้ที่ใต้ตาราง

(5) เชิงอรรถ (footnotes) ของตารางจะเขียนไว้ใต้ตารางหรือใช้เครื่องหมายดอกจัน (*) เพื่อแสดงความหมายของค่าหรือข้อมูลทางสถิติ

- **รูปภาพ (figures)**

(2) ให้ใช้โปรแกรมกราฟฟิกคอมพิวเตอร์ในการวาดรูป

(3) รูปภาพที่เป็นลายเส้นควรใช้รูปแบบ EPS ในการวาดเส้นรูปภาพและรูปภาพที่เป็นโทนสีควรใช้รูปแบบ TIFF ในการไล่เฉดสี

(4) รูปภาพทุกรูปจะต้องมีหมายเลขและคำบรรยายภาพกำกับไว้ใต้ภาพ โดยใช้ชื่อรูปภาพเป็น “Fig” ตามด้วยลำดับที่ของรูปภาพ เช่น “Fig1” เป็นต้น

- **เอกสารอ้างอิง (references)** เรียงลำดับเลขการอ้างอิงตามเอกสารอ้างอิงท้ายบทความ และใช้ตาม Vancouver style การอ้างอิงถึงชื่อบุคคล ถ้ามีผู้เขียนมากกว่า 6 คน ให้ใส่ชื่อ 6 คนแรก แล้วตามด้วย et al. ส่วนการเขียนเอกสารอ้างอิง

ท้ายบทความ การย่อชื่อวารสารให้ใช้ตาม Index Medicus โดยศึกษาได้ในเว็บไซต์ http://www.medscape.com/home/search/indexMedicus/IndexMedicus-A.html

กรุณาลงนามในแบบฟอร์มการส่งบทความเพื่อขอตีพิมพ์ เพื่อแสดงว่าผู้เขียนได้อ่านเกณฑ์การเขียนบทความทั้งหมด

- **ตัวอย่างการเขียนเอกสารอ้างอิง (references) กรุณาดูในหัวข้อ “ Instruction to authors ”**

The Thai Journal of Orthopaedic Surgery

Acknowledgements to Reviewers 2013

Pongsak Yuktanandana
Editor in Chief

We are fortunate to have an outstanding group of reviewers who kindly volunteer their time and effort to review manuscripts for *The Thai Journal of Orthopaedic Surgery*. They are critical team players in the continued success of the journal, ensuring a peer review process of the high integrity and quality. The editor would like to thank the following reviewers who provided their expertise in evaluating manuscripts for *The Thai Journal of Orthopaedic Surgery* during 2013. A special thanks goes to Supawinee Pattanasoon for being our managing editor.

List of reviewers:

Theerachai Apivatthakakul
Sakda Chaikitpinyo
Cholawish Chanlalit
Sukrom Cheecharern
Bavornrit Chuckpaiwong
Sittisak Honsawek
Wiroon Laupattarakasem
Supphamard Lewsirirat
Sirichai Luevitoonvechkij
Thomas Mabey
Banchong Mahaisavariya
Jakravoot Maneerit
Vinai Parkpian
Vajara Phiphobmongkol
Chathchai Pookarnjanamorakot
Sattaya Rojanasthien
Sukit Saengnipanthkul
Nadhaporn Saengpetch
Thananit Sangkomkamhang
Thawee Songpatanasilp
Aree Tanavalee
Boonsin Tangtrakulwanich
Patarawan Woratanarat
Pongsak Yuktanandana