# Arthroscopic synovectomy for pigmented villonodular synovitis of the knee: recurrence rate and functional outcomes after a 4-year follow-up Ahmed H. Wally

Department of Orthopaedic Surgery and Traumatology, Alexandria University, Alexandria, Egypt

Correspondence to Ahmed H. Waly, 20 Mahmoud El Deeb Street, Zezenya, Alexandria, 53213, Egypt. Tel: +20 122 218 6065; e-mail: drwaly28@gmail.com

Received: 5 November 2019 Revised: 20 November 2019 Accepted: 25 November 2019 Published: 24 June 2021

**The Egyptian Orthopaedic Journal** 2020, 55:33–39

# Context

Pigmented villonodular synovitis (PVNS) is a rare proliferative pathology of synovial joints mainly affecting the knee. Arthroscopic synovectomy has much lower morbidity than open synovectomy.

#### Aims

The objectives of the study were to evaluate the rate of recurrence and the function outcome after arthroscopic synovectomy for PVNS.

# Settings and design

A retrospective study was held at Alexandria University.

#### Patients and methods

A retrospective study included all patients between 2010 and 2012 with PVNS of the knee. They were all treated by synovectomy followed by a chemical synoviorthesis in the case of residual lesions. Lysholm score was used for assessment of the results. The series included 28 patients, comprising 20 men and eight women, with mean age of 41±12 years.

#### Statistical analysis

SPSS, version 20.0, was used.

#### Results

At mean follow-up of 4 years, 28 patients were reviewed (18 nodular and 10 diffuse). Only two case had recurrence. It was a diffuse form. Recurrence occurred after one and half years in one case and after 2 years in the second case. After revision synovectomy, no recurrence occurred. The mean Lysholm score improved from preoperative value of 62.5±8 points to 91±8 (P<0.01). The mean preoperative visual analog scale score improved from 41.5 to 95 points (P<0.01).

# Conclusion

Arthroscopic synovectomy revealed satisfactory control of the disease, and it preserved the function of the knee. In diffuse forms and recurrence forms, the patient's chances of recovery are still possible.

# Keywords:

arthroscopic synovectomy, knee effusion, pigmented villonodular synovitis

Egypt Orthop J 55:33-39

© 2021 The Egyptian Orthopaedic Journal 1110-1148

# Introduction

Pigmented villonodular synovitis (PVNS) is a benign idiopathic proliferative pathology of the synovial membrane [1]. PVNS affects people in their third or fourth decades of life, affecting men and women in equal proportions. In most cases, the disease is monoarticular and involves mainly the knee joint; the hip and ankle joints follow in frequency. It has the potential to extensively invade local structures such as muscles, tendons, cartilage, bones, and skin [2].

Without treatment, PVNS results in rapid and irreversible joint destruction. In 1967, Granowitz *et al.* [3] distinguished two intraarticular macroscopic forms, that is, localized (nodular) and diffuse, which involve the entire synovium. Extra-articular extension to the adjacent muscular and tendon structures is sometimes found, most often in diffuse forms.

Joint aspiration reveals a brownish discoloration of the fluid owing to the breakdown of blood products (hemosiderin) within the joint [4]. The classical appearance of PVNS on plain radiograph films is of a soft-tissue swelling or mass about the joint, with joint-space preservation. Peri-articular osteoporosis is not commonly seen. Erosions or subchondral cysts are common and are more prevalent when PVNS occurs at 'tight' joints such as the hip, ankle, or elbow in comparison with the knee [5].

MRI will show the effusion, and the hemosiderinladen soft-tissue masses will be seen as areas of low

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

signal intensity on T1 and especially on T2 sequences. The signs in favor of a PVNS are thickened synovial, heterogeneous, enhancement by the injection of Gadolinium, and including hyposignal plaques corresponding to deposits of hemosiderin in the joint [6].

Pathologically, the lesion shows dense infiltrate of polygonal or spindle cells with abundant cytoplasm and vesicular nuclei; some of the cells contain hemosiderin. Multinucleated giant cells are sometimes present, either scarcely or in large numbers. Aggregation of foamy cells can also be seen. Abundant production of collagen, fibrosis, and hyalinization may be evident in patients with long-standing disease [7].

The pathogenesis of PVNS is not clear; however, most authors believe it is caused by chronic inflammation. Others think it is a neoplastic disorder such as a giant cell sarcoma arising near or inside the synovial space or tendon sheath [2]. A study by Ijiri *et al.* [8] suggested that human peptide, a material that interferes with apoptotic activity, is present in the diffuse form of the disease but is less commonly present in the nodular form.

The gold standard treatment of PVNS is the surgical excision of all the lesions. In diffuse forms, the treatment usually adopted is total open synovectomy, whereas arthroscopic synovectomy is most often reserved for localized nodular forms [9]. In contrast to open synovectomy, arthroscopic synovectomy appears to preserve knee function with a low local recurrence rate and few complications [10]. Adjuvant treatment modalities such as external beam radiation and intraarticular injection of yttrium-90 have been tried and shown to be effective in reducing the rate of local recurrence with acceptable joint damage. The main

long-term goal is to eradicate the synovial disease while avoiding the need for joint replacement [11].

The aim of this study was to evaluate the results of arthroscopic synovectomy, for both localized and diffuse PVNS. The hypothesis of the study was that arthroscopic synovectomy would preserve the function of the knee while obtaining a low rate of local recurrence.

# Patients and methods

A retrospective study was performed at El Hadara University Hospital. The study was approved by the institutional ethics committee in the Orthopedic Department of Orthopaedic Surgery, Alexandria University, Egypt. The inclusion criteria were any patient who had an arthroscopic synovectomy of a histologically proven knee PVNS between 2010 and 2012. The exclusion criteria were extra-articular extension and/or open synovectomy. Recurrence after arthroscopic synovectomy was included.

During this period, 28 patients were operated upon, comprising 20 men and eight women, with a mean age of 40.5 years (32–47 years). Ten (35%) patients had a diffuse and 18 (65%) had a nodular form, all without extra-articular extension nor bony destruction evident on preoperative radiographs. At the time of diagnosis, 18 had right knee affection and 10 had left side. All patients were evaluated clinically and radiologically. They were subjected to preoperative radiographs and MRI. Only two cases had recurrence after arthroscopic synovectomy (Table 1).

There were 18 (65%) patients with nodular form. In 50% of them, the lesion was located in the suprapatellar pouch and 22% in the medial gutter. Overall, 11% of

	Diffuse variety [n (%)] Nodular variety [n (%		
Number	10 (35)	) 18 (65)	
		9 suprapatellar pouches	
		2 anterolateral	
		4 posterior compartments	
		3 medial gutter	
Age	42 years (36–47 years)	39 years (32–41 years)	
Sex	10 males (100)	10 males (56)	
		8 females (44)	
Side	6 right (60)	12 right (67)	
	4 left (40)	6 left (34)	
Preoperative flexion	110±7 deg.	126±12 deg.	
Preoperative Lysholm score	57±8 points	68±10 points	
Preoperative VAS score	39 points	44 points	
Mean duration of symptoms prior to presentation	8 months (1–13 months)	10 months (2–12 months)	

 Table 1 Demographic data of the patients involved in the study

VAS, visual analog scale.

the nodules were found in the anterolateral part of the knee with extension to fat pad and femoral trochlea and 16% were infiltrating the medial gutter only (Fig. 1).

The mean preoperative flexion was 126±12°. MRI was performed in all patients, showing the signs in favor of a PVNS (Fig. 2): thickened synovial, heterogeneous, enhancement by the injection of gadolinium, and including hyposignal plaques corresponding to deposits of hemosiderin in the joint [6]. All cases had histological evidence of PVNS postoperatively.

In all cases, a 30° arthroscope was used. A synovial biopsy was performed. The synovectomy was

## Figure 1



The distribution of the nodular form group (n=18 patients).

#### Figure 2



MRI T1 FSE image, showing a diffuse form of PVNS in a 42-year-old female patient. PVNS, pigmented villonodular synovitis.

performed with a motorized shaver with 4.5- and 5.5mm blade (Fig. 3). The three standard approaches (anteromedial, anterolateral, and superolateral) were used. Posterior synovectomy was performed only in diffuse forms and nodular forms with posterior lesions on MRI through the posteromedial and posterolateral lateral portals. The posteromedial approach was performed by transillumination. Postoperative chemical synoviorthesis was done in all cases using triamcinolone hexacetonide (Kenacort).

Postoperative protocol was as follows: all patients had an intraarticular drain removed after 24 h after surgery. Passive and active rehabilitation was started from the first postoperative day and prolonged for 1 month. A knee extension splint was kept between sessions for a month to avoid flexion deformity. Each patient was reviewed at 1, 3, 6, and 12 months postoperatively and once a year thereafter.

At the last follow-up (4 years), all patients were reviewed clinically using the Lysholm score [12]. According to the Lysholm-Tegner score, the results were classified to be poor (0-64), average (65-83), or excellent (84–100). The mean preoperative Lysholm score was  $62.5\pm8$  points. The mean preoperative visual analog scale score was 41.5 points. The functional evaluation was performed using the standard system of the Musculoskeletal Tumor Society with the modifications developed by Enneking *et al.* [13], which is based on six parameters, including an assessment of pain, functional activities, emotional acceptance, the need for use of external support, walking ability, and gait.

### Figure 3



A 5.5-mm motorized shaver used for arthroscopic synovectomy from suprapatellar pouch.

# Statistical analysis

Statistical analysis was done using SPSS software (version 20.0; SPSS Inc., Chicago, Illinois, USA). Owing to the size of the sample, nonparametric tests were used. The quantitative variables were tested by the Mann–Whitney test or the Wilcoxon test for matched groups. The significance threshold was set at 0.05.

# Results

No patients was lost to follow-up. The mean duration of follow-up was 4 years. Only two cases had recurrence. The first was after one and half years and the second was after 2 years. Both had diffuse PVNS form and were revised using arthroscopic synovectomy. At the last follow-up of the second intervention, no recurrence was noticed.

The most common symptom was discomfort of the knee (100% of the patients) followed by swelling (90%) and locking episodes of the knee (65%) in cases of nodular forms. In all patients, the histological examination confirmed the diagnosis of PVNS. All plain radiographs were normal even in patients having long-term symptoms.

The mean Lysholm improved from score preoperative value of 62.5±8 points to 91±8 (P < 0.01). The mean preoperative visual analog scale score improved from 41.5 to 95 points (P<0.01). The median Lysholm score was 90±7 in the diffuse group and 92±10 in the localized group (P>0.05) (Fig. 4). The final scores were excellent. The mean postoperative flexion increased to 150±2 for diffuse form and to 155±7° in nodular form (P<0.05). No patients had flexion deformity postoperatively (Table 2).

There were no complications reported after synovectomy. There were no postoperative infections, no portal healing problems, no stiffness, and no deep vein thrombosis.

# Discussion

The mainstay of PVNS treatment is surgical or arthroscopic synovectomy. Arthroscopic synovectomy has reduced morbidity and is well tolerated by patients. Open surgical synovectomy causes stiffness and pain and has a long recovery time, mainly after procedures involving the knee joint. However, the relapse rates of both approaches are reported to be relatively high, ranging between 8 and 46% [14].

The incidence of postoperative stiffness after open synovectomy ranges between 24% for Flandry *et al.* [15] and 50% in the Johansson *et al.* [16]. The arthroscopic synovectomy allows the removal of a maximum number of lesions while probably offering a functional advantage over open surgery and a low rate of postoperative complications. However, arthroscopic surgical treatment is highly specialized and has a long and difficult learning curve [17].

#### Figure 4





#### Table 2 Postoperative data at the final follow-up

	Diffuse		Nodular		
	Preoperative	Postoperative	Preoperative	Postoperative	P value
Lysholm score	57±8 points	90±7 points	68±10 points	92±10 points	< 0.05
VAS score	39 points	94 points	44 points	95 points	< 0.05
Flexion	110±7°	150±2°	126±12°	155±7°	< 0.05
Recurrence	2 (20)		None		
Final FU modified Enneking Musculoskeletal Tumor Society	85		92		

VAS, visual analog scale.

This study shows that arthroscopic synovectomy for PVNS has a lesser complication rate and results in a globally low rate of local recurrence and preserves joint function. Unlike localized forms with a low or no recurrence rate, diffuse forms often recur whatever the treatment [18].

Ottaviani *et al.* [19] performed a retrospective study over 122 cases of PVNS. Overall, 89% were diffuse form. PVNS was analyzed with a mean follow-up of  $5.8\pm4.3$  years. All cases were done by open synovectomy. The relapse rate was 30% in knee cases. They were all diffuse form with a mean delay before relapse of  $2.6\pm2.4$  years.

Sharma *et al.* [20] investigated the functional outcome of 17 PVNS of the knee at 6-year mean follow-up. The mean age was 33 years (range, 16–58 years) with a slight male predominance. The lesion was predominantly anterior in nine patients, posterior in four, anterolateral in two, and medial and lateral in one each. Three patients (four knees) had localized disease and 13 diffuse. Removal of a localized synovial mass or loose body with surrounding partial synovectomy (four) was carried out for the localized variety, whereas open partial (three) or total (radical) synovectomy (10) was performed in all cases of diffuse PVNS. Three (23%) of the 17 knees had a recurrence, noted at 4, 6, and 8 years postoperatively. They were all diffuse form.

In this study, the results were comparable to the literature. There were no cases of recurrence in the nodular form. However, in the diffuse form group, the recurrence rate of our series was two (20%) cases, which is less than the open synovectomy results: 25% for Schwartz *et al.* [7], 33% for Johansson *et al.* [16], and 46% for Byers *et al.* [21]. The best results are those obtained by Flandry *et al.* [15], with a recurrence rate of 8%.

Regarding arthroscopic synovectomy results, De Ponti et al. [9] retrospectively examined the results of arthroscopic synovectomy of PVNS of the knee in 19 patients, with an average follow-up of 60 months (minimum, 12; maximum, 128). Four patients were affected by localized PVNS and were subject to partial synovectomy with excision of the pathologic tissue. The remaining 15 patients presented a diffuse form of PVNS; seven of them underwent extended arthroscopic synovectomy and eight underwent partial synovectomy. In the group affected by the localized form of PVNS, the arthroscopic local excision resulted in a complete and persistent regression of the pathology. Among the patients affected by the diffuse form of PVNS, clinical results were better and the recurrence rate was lower in the group treated with extended synovectomy. No relevant complications were encountered.

Moreover, Kim *et al.* [22] investigated the results of arthroscopic synovectomy for localized PVNS of the knee in 11 patients between the ages of 15 and 59 years (mean, 34.6 years). The most common involved site was the anteromedial synovium near the anterior horn of the medial meniscus (five patients). The remaining cases were located in the anterior fat pad (two patients), suprapatellar pouch, posteromedial compartment, medial gutter, and the anterior horn of the lateral meniscus. Nine patients had one mass, and the remaining patients each had two or three masses. There was no evidence of recurrence at follow-up for an average of 29.9 months (range, 24–48 months).

Loriaut *et al.* [23] investigated the outcome of arthroscopic treatment of nodular PVNS of the knee in 20 patients. The average follow-up was 75 months (range, 12–144). The median age of the patients was 46 years (range, 23–71). The nodules were localized in the gutters (45%), suprapatellar pouch (26%), patellar fat pad (13%), posterior compartment of the knee (13%), and in the femoral notch (9%). Four patients had recurrent disease. Two patients had clinical symptoms that occurred at 12 and 50 months after the first surgery.

Sharma and Cheng [24] retrospectively reviewed the outcomes of PVNS in 49 patients (12 localized and 37 diffuse) who were treated with synovectomy, with a mean age of 35.2 years (range, 10-73). Minimum follow-up was 1 year (mean, 6.2 years; range, 1-13). A total of 21 patients had a relapse. The recurrencefree survival was 95% for open versus 62% for arthroscopic synovectomy at 2 years, and 71 and 41% at 5 years. The recurrence-free survival was 91% for localized and 70% for diffuse PVNS at 2 years, and 73 and 48% at 5 years. Diffuse disease (RR=4.49)arthroscopic and synovectomy (RR=3.30) were associated with relapse.

# **Functional outcomes**

In this series, the mean functional scores are excellent for both nodular and diffuse PVNS. No significant difference was found between these two groups. Loriaut *et al.* [23] reviewed 20 patients who were operated arthroscopically for localized PVNS; the mean Lysholm score was 'good' at the last follow-up (mean, 85.5, range, 83–88 points). Nassar *et al.* [2] followed up 12 cases of PVNS for a mean of 27 months using modified Enneking Musculoskeletal Tumor Society score. The functional outcome of the involved joint in all patients was excellent so far according to Enneking's criteria. The average postoperative score was 85% (80–90%). In the current series, similar results were obtained with average postoperative Enneking score of 85% for the diffuse form and 92% for the nodular form.

## Adjuvant therapies

Postsynovectomy adjuvant treatment with external beam radiation therapy or intraarticular injection of yttrium-90 are two adjuvant therapies that have yielded better results compared with surgical excision alone [25]. The external radiation associated with a complete synovectomy seems to give good results especially in the forms with high risk of recurrence [26]. Nassar et al. [2] used postsynovectomy external beam radiation therapy for PVNS of 12 knees 6-8 weeks after surgery. They followed their cases up for 27 months, with no single case of recurrence. All their cases were diffuse form. However, Jahangier et al. [27] reported that the overall success rate of postsynovectomy radiation using 90Y was 75% in 83 patients.

The chemical synoviorthesis with triamcinolone was also used as adjuvant therapy after PVNS arthroscopic synovectomy [19,28,29]. In this study, chemical synoviorthesis was carried out in all patients. There were two cases of local recurrence. They were both diffuse forms. Pannier *et al.* [29] used chemical synoviorthesis in six cases. Recurrence was noted in two diffuse forms, one at 10 months and other after 24 months after surgical synovectomy.

## Limitations of the study

There are several limitations of this study. First, it is a retrospective study with low evidence power. Second, given the extremely low incidence of this condition, the number of patients is certainly low.

# Conclusion

Arthroscopic synovectomy for both nodular and diffuse forms with a superadded chemical synoviorthesis allows a satisfactory control of the PVNS while preserving the function of the knee. In diffuse forms, the patient's chances of recovery are preserved.

# Financial support and sponsorship Nil.

# Conflicts of interest

There are no conflicts of interest.

#### References

- Dwidmuthe S, Barick D, Rathi T, Park PR. Arthroscopic management of pigmented villonodular synovitis of the knee joint. J Orthop Case Rep 2015; 5:15–17.
- 2 Nassar WA, Bassiony AA, Elghazaly HA. Treatment of diffuse pigmented villonodular synovitis of the knee with combined surgical and radiosynovectomy. HSS J 2009; 5:19–23.
- 3 Granowitz SP, D'Antonio J, Mankin HL. The pathogenesis and long-term end results of pigmented villonodular synovitis. Clin Orthop Relat Res 1976; 114:335.
- 4 Rao AS, Vigorita V. Pigmented villonodular synovitis (giant-cell tumor of the tendon sheath and synovial membrane). A review of eighty-one cases. J Bone Joint Surg Am 1984; 66:76–94.
- 5 Dorwart R, Genant H, Johnston W, Morris J. Pigmented villonodular synovitis of synovial joints: clinical, pathologic, and radiologic features. Am J Roentgenol 1984; 143:877–885.
- 6 Mandelbaum BR, Grant TT, Hàrtzman S, Reicher MA, Flannigan B, Bassett LW, et al. The use of MRI to assist in diagnosis of pigmented villonodular synovitis of the knee joint. Clin Orthop Relat Res 1988; 231:135–139.
- 7 Schwartz HS, Unni KK, Pritchard DJ. Pigmented villonodular synovitis: a retrospective review of affected large joints. Clin Orthop Relat Res 1989; 247:243–255.
- 8 Ijiri K, Tsuruga H, Sakakima H, Tomita K, Taniguchi N, Shimoonoda K, et al. Increased expression of humanin peptide in diffuse-type pigmented villonodular synovitis: implication of its mitochondrial abnormality. Ann Rheum Dis 2005; 64:816–823.
- 9 De Ponti A, Sansone V, Malcherè M. Result of arthroscopic treatment of pigmented villonodular synovitis of the knee. Arthroscopy 2003; 19:602–607.
- 10 Aurégan J-C., Klouche S, Bohu Y, Lefèvre N, Herman S, Hardy P. Treatment of pigmented villonodular synovitis of the knee. Arthroscopy 2014; 30:1327–1341.
- 11 Franssen M, Boerbooms A, Karthaus R, Buijs W, Van De Putte L. Treatment of pigmented villonodular synovitis of the knee with yttrium-90 silicate: prospective evaluations by arthroscopy, histology, and 99mTc pertechnetate uptake measurements. Ann Rheum Dis 1989; 48:1007–1013.
- 12 Tegner Y, Lysholm J. Rating systems in the evaluation of knee ligament injuries. Clin Orthop Relat Res 1985; 198:42–49.
- 13 Enneking WF, Dunham W, Gebhardt MC, Malawar M, Pritchard DJ. A system for the functional evaluation of reconstructive procedures after surgical treatment of tumors of the musculoskeletal system. Clin Orthop Relat Res 1993; 286:241–246.
- 14 Adem C, Sebo TJ, Riehle DL, Lohse CM, Nascimento AG, Recurrent and nonrecurrent pigmented villonodular synovitis 1. Nat Med Libr 2002; 22:448–452.
- 15 Flandry FC, Hughston JC, Jacobson KE, Barrack RL, Mccann SB, Kurtz DM. Surgical treatment of diffuse pigmented villonodular synovitis of the knee. Clin Orthop Relat Res 1994; 300:183–192.
- 16 Johansson JE, Ajjoub S, Coughlin LP, Wener JA, Cruess RL. Pigmented villonodular synovitis of joints. Clin Orthop Relat Res 1982; 163:159–166.
- 17 Louisia S, Charrois O, Beaufils P. Posterior 'back and forth' approach in arthroscopic surgery on the posterior knee compartments. Arthroscopy 2003; 19:321–325.
- 18 Pinaroli A, Aït SST, Servien E, Neyret P. Surgical management of pigmented villonodular synovitis of the knee: retrospective analysis of 28 cases. Rev Chir Orthop Reparatrice Appar Mot 2006; 92:437–447.
- 19 Ottaviani S, Ayral X, Dougados M, Gossec L. Pigmented villonodular synovitis: a retrospective single-center study of 122 cases and review of the literature. Semin Arthritis Rheum 2011; 40:539–546.
- 20 Sharma H, Rana B, Mahendra A, Jane M, Reid R. Outcome of 17 pigmented villonodular synovitis (PVNS) of the knee at 6 years mean follow-up. Knee 2007; 14:390–394.
- 21 Byers P, Cotton RE, Deacon O, Lowy M, Newman P, Sissons H, et al. The diagnosis and treatment of pigmented villonodular synovitis. Bone Joint J 1968; 50:290–305.
- 22 Kim S-J., Shin S-J., Choi N-H., Choo E-T. Arthroscopic treatment for localized pigmented villonodular synovitis of the knee. Clin Orthop Relat Res 2000; 379:224–230.
- 23 Loriaut P, Djian P, Boyer T, Bonvarlet J-P., Delin C, Makridis KG. Arthroscopic treatment of localized pigmented villonodular synovitis of the knee. Knee Surg Sports Traumatol Arthrosc 2012; 20:1550–1553.

- 24 Sharma V, Cheng EY. Outcomes after excision of pigmented villonodular synovitis of the knee. Clin Orthop Relat Res 2009; 467:2852–2858.
- 25 Shabat S, Kollender Y, Merimsky O, Isakov J, Flusser G, Nyska M, et al. The use of surgery and yttrium 90 in the management of extensive and diffuse pigmented villonodular synovitis of large joints. Rheumatology 2002; 41:1113–1118.
- 26 O'Sullivan B, Cummings B, Catton C, Bell R, Davis A, Fornasier V, et al. Outcome following radiation treatment for high-risk pigmented villonodular synovitis. Int J Radiat Oncol Biol Phys 1995; 32:777–786.
- 27 Jahangier Z, Jacobs J, Van Isselt J, Bijlsma J. Persistent synovitis treated with radiation synovectomy using yttrium-90: a retrospective evaluation of 83 procedures for 45 patients. Rheumatology 1997; 36:861–869.
- 28 Gumpel J, Shawe D. Diffuse pigmented villonodular synovitis: non-surgical management. Ann Rheum Dis 1991; 50:531.
- 29 Pannier S, Odent T, Milet A, Lambot-Juhan K, Glorion C. Pigmented villonodular synovitis in children: review of six cases. Rev Chir Orthop Reparatrice Appar Mot 2008; 94:64–72.