Outcomes after Excision of Pigmented Villonodular Synovitis of the Knee

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Abstract Pigmented villonodular synovitis (PVNS) has a high but variable recurrence rate. Prior studies do not compare recurrence-free survival (RFS) for various surgical approaches or salvage surgery for relapse. We therefore determined: (1) RFS after excision; (2) RFS after salvage surgery for relapse; (3) factors associated with relapse. We retrospectively reviewed the medical records of 49 patients with previously untreated PVNS of the knee (12 localized, 37 diffuse) who were treated with synovectomy from 1991 to 2008; there were 22 males and 27 females, with mean age of 35.2 years (range, 10–73). Minimum followup was 1 year (mean, 6.2 years; range, 1–13). Twenty-one patients had a relapse. The RFS for index surgery was 75% and 53%; and for salvage surgery was 71% and 52% at 2 and 5 years respectively. The RFS was 95% for open versus 62% for arthroscopic synovectomy at 2 years, 71% and 41% at 5 years. The RFS was 91% for localized and 70% for diffuse PVNS at 2 years, 73% and 48% at 5 years. Diffuse disease (RR = 4.49) and arthroscopic synovectomy (RR = 3.30) were associated with relapse. Recurrence was frequent after synovectomy. Re-excision can salvage relapses as successfully as excision

for primary disease; however, morbidity was associated with additional surgeries.

Level of Evidence: Level IV, therapeutic study. See Guidelines for Authors for a complete description of levels of evidence.

Introduction

Pigmented villonodular synovitis (PVNS) was once believed to be an inflammatory reaction to an unknown cause [13]. Evidence of monoclonal origin (DNA replication from single ancestral cell) and centrifugal (tumor-like cell proliferation from center to periphery) growth patterns with capacity to erode surrounding tissues suggests a neoplastic process [10]. Despite its benign histological appearance, PVNS has a high but variable recurrence rate of 8% to 60% [3, 4, 6, 9, 11, 15–17, 19, 20, 25]. Recurrences after the initial surgery have been a major concern, particularly in large joints and for the diffuse type of PVNS [4, 19]. PVNS is locally aggressive, spreading to surrounding synovial tissues and invading adjacent soft tissue structures and bone [10]. There have been rare reports of malignant transformation and metastasis [2]. The use of more extensive approaches and adjuvant radiotherapy (external beam or intraarticular radiocolloid injection) reportedly improves local control [6, 22, 24].

The literature suggests different factors responsible for recurrence, the most important of which include a history of previous surgery for PVNS of that joint, diffuse type of disease, large joints, and adequacy of the synovectomy [5, 19]. The rarity of the disease greatly hampers the ability to perform a prospective study in a controlled manner; hence, prior published studies on PVNS provide Level IV evidence regarding the treatment outcomes [21]. A variety of

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approaches have been proposed for treating PVNS. Several options have been an all arthroscopic procedure [9, 15–17, 25], an extensile open anteroposterior approach [6, 11], a combined anterior arthroscopic and open posterior synovectomy [9], and a subtotal synovectomy with adjuvant radiotherapy [3, 20].

Given the limited information on recurrences we determined: (1) the RFS after excision; (2) whether relapse can be salvaged with reexcision; and (3) factors associated with relapse.

Materials and Methods

We retrospectively reviewed the medical records of all 49 consecutive patients of previously untreated PVNS of the knee treated with excision without adjuvant radiation between 1991 and 2008. There were 20 male and 29 female patients with an average age of 35.2 years (range, 10–73 years) at the time of diagnosis. The main principle of treatment was to resect all the diseased tissue visible on inspection using either arthroscopic or open techniques involving the anterior, posterior, or both compartments. The localized disease type was treated by marginal resection and the diffuse disease was treated with intralesional resection with excision of all the macroscopic disease. The choice of surgery depended on the tumor extent on the magnetic resonance imaging (MRI) performed during the surgeon's preoperative evaluation. All patients were examined preoperatively with standing anteroposterior and lateral radiographs of the knee. MRI was used preoperatively to assess the extent of the disease. Tumors were classified as diffuse or localized (Figs. 1, 2). Thirty-seven patients had diffuse disease and 12 patients

had localized disease. Patients were monitored for local relapse through followup clinical examination and MRI. The postoperative followup protocol included clinic visits at 2 weeks, 3 months, 6 months, 1 year and then yearly. MRI was performed at the 6 month postoperative visit. Further MRI examination was only performed if the patient presented with symptoms such as pain and effusion suggestive of local recurrence. The minimum followup was 1 year (average, 6.2 years; range, 1–13 years). The minimum followup for the salvage synovectomy was 14 months (average, 5.4 years; 1.2–11.5 years). We had prior IRB approval for our study. No patients were lost to followup.

We divided the patients into three groups depending on the surgical technique (Fig. 3). Group A: Eighteen patients were treated with anterior arthroscopic synovectomy as the initial treatment (five nodular, 13 diffuse). Group B: Eight patients underwent anterior arthroscopic synovectomy and open posterior synovectomy for diffuse PVNS. Group C: Twenty-three patients were treated with open surgery as the initial surgery. Sixteen of these patients had diffuse disease and were treated with open anterior and posterior synovectomy. The seven remaining patients had localized disease restricted to either anterior or posterior compartment. The treatments included either open anterior synovectomy (four patients) or open posterior synovectomy (three patients). Overall, in the three groups there were 12 patients with localized PVNS and 37 patients with diffuse PVNS.

Kaplan-Meier life table survivorship analysis [14] was performed to determine the local recurrence-free survival

Fig. 1 This axial MRI of the knee shows a diffuse type of PVNS.

Fig. 2 This axial MRI of the knee shows a localized type of PVNS in the suprapatellar pouch.

Fig. 3 The flowchart shows the distribution of the PVNS cases according to their disease subtype and the type of surgical synovectomy.

Table 1. Recurrence-free survival (RFS)

Group	2 Years	5 Years	
Overall	75% (63 to 88)	53% (36 to 71)	
Open synovectomy (group C)	95% (86 to 100)	71% (46 to 96)	p = 0.007
Arthroscopic synovectomy (groups A + B)	62% (42 to 82)	41% (17 to 64)	
Salvage open synovectomy	71% (50 to 93)	53% (29 to 77)	p = 0.69*
Diffuse PVNS	70% (55 to 86)	48% (28 to 68)	
Localized PVNS	91% (74 to 100)	73% (38 to 100)	p = 0.063
Anterior arthroscopic synovectomy → Group (A)			
Anterior arthroscopic synovectomy + open posterior synovectomy → Group (B)			
Open anterior and posterior synovectomy → Group (C)			

* p-Value for comparison of overall (Index) surgery and salvage open surgery.

(defined as the time from the surgical excision to local recurrence as determined by MRI) after the initial surgical treatment as well as after a salvage procedure following local relapse. Log-rank tests were used to compare the RFS after arthroscopic versus open synovectomies and RFS for diffuse versus localized disease. For KM analysis we combined the patients treated with anterior arthroscopic synovectomy (Group A) and those treated with anterior arthroscopic and posterior open synovectomy (Group B) into one group (Group A + B) (Table 1). This group was compared to open anterior and open posterior synovectomy in the second group (Group C). Cox multivariate regression [8] was performed to determine the relative risk (RR) of individual factors associated with relapse, such as patient's age at presentation (years), gender, tumor subtype (diffuse or nodular), and type of surgery (open, arthroscopic, or combined).

Results

The overall recurrence-free survival was 75% ± 13% at 2 years and 53% ± 18% at 5 years (Table 1; Fig. 4). The recurrence-free survival at 2 years was 62% for Group A + B and 95% for Group C, and 40% and 71% at 5 years respectively (Fig. 5). The RFS after excision was greater ($p = 0.0071$), both at 2 and 5 years, in the group which had complete open synovectomy. Twelve of 13 patients with diffuse PVNS treated with arthroscopic anterior synovectomy had a relapse compared to relapse in about 1/3 of the patients treated with open anterior and posterior synovectomy. Arthroscopic synovectomy had lower ($p = 0.019$) recurrence rate for localized disease than diffuse disease (Fig. 6). There were 16 recurrences in 26 arthroscopic synovectomies and five recurrences in 23 open synovectomies. The recurrence-free survival at 2 years was 91%

Fig. 4 The graph shows the KM analysis for the recurrence-free survival (RFS) of all PVNS patients after surgical synovectomy.

Fig. 7 A comparison of the RFS between nodular and diffuse disease-subtype of PVNS in all patients is shown.

Fig. 5 A comparison of the RFS between open and arthroscopic synovectomy for PVNS of the knee is shown.

Fig. 6 A comparison of the RFS between nodular and diffuse disease-subtype treated by arthroscopic synovectomy is shown.

Fig. 8 A sagittal MRI of the knee demonstrating PVNS in the posterior compartment is shown.

for localized disease and 70% for diffuse disease and 73% and 48% respectively at 5 years (Fig. 7). The recurrence rate was higher ($p = 0.06$) for diffuse PVNS as compared to localized PVNS (Table 1). There were four recurrences in 12 patients with localized disease as compared to 17 relapses in 37 patients with diffuse PVNS. The excision of posterior disease (Fig. 8) in the diffuse subtype demonstrated a trend towards improved ($p = 0.15$) recurrence free survival in these patients compared to patients who did not get posterior synovectomy for posterior disease (Fig. 9).

Overall, 21 patients underwent salvage surgery for local recurrence. The highest recurrence was in the group of patients with diffuse type of disease treated with anterior arthroscopic synovectomy. The recurrence-free survival for the salvage synovectomy was $71\% \pm 21\%$ at 2 years and

Fig. 9 A comparison of the RFS between synovectomy with and without addressing posterior disease in diffuse PVNS is shown.

Fig. 10 A comparison of the RFS between primary and salvage surgical synovectomy for PVNS of the knee is shown.

52% $\pm$ 24% at 5 years compared to 75% $\pm$ 13% at 2 years and 53% $\pm$ 18% at 5 years for the primary synovectomy (Table 1). The RFS after primary and salvage synovectomy showed similar trend ($p = 0.63$) at both 2 and 5 years after surgery (Fig. 10).

The type of surgery and the disease subtype were associated with relapse. The arthroscopic synovectomy ($p = 0.010$; RR = 3.30) and diffuse type of disease ($p = 0.044$; RR = 4.49) were associated with decreased recurrence-free survival. We observed no association of relapse with age or gender.

Discussion

The existing literature on PVNS of the knee suggests a variable recurrence rate after excision. No single study

compares RFS after synovectomy via various surgical approaches or determines RFS after salvage synovectomy for local recurrence. The specific goals of our study were: (1) to determine RFS after excision comparing various surgical approaches; (2) to determine if recurrence can be salvaged with reexcision; and (3) to determine factors associated with recurrence.

We note several limitations to our study. First is the low power with a relatively small number of patients. This particular limitation may affect the assessment of factors associated with local recurrence. However, the low incidence of the disease makes larger studies difficult, especially addressing only knee. Second, selection bias is inherent in this retrospective series with the worst disease on the MRI treated with open surgery. However, despite the bias that would predict a higher relapse for open surgery, we found the reverse: open surgery patients had a lower relapse rate. Third is the lack of clinical outcome scores. However, the local relapse of the disease was documented with MRI and was treated with reexcision in symptomatic patients. Finally, we excluded patients with PVNS in other joint areas of the body so our results can likely be extrapolated only for PVNS of the knee.

When arthroscopic synovectomy is incomplete/subtotal, recurrence rates may be as high as 50% to 60% [7, 9, 17]. In our study as well, the recurrence was highest for diffuse PVNS treated with subtotal arthroscopic synovectomy and compared with recurrence rates in the literature (Table 2). In the hands of an experienced arthroscopic surgeon, however, arthroscopic total synovectomies with the use of both anterior and posterior portals may have a similar if not better prognosis (9%-20% recurrence) compared to open procedures [25]. Open synovectomy with anterior and posterior approach reportedly has a recurrence rate of 8% to 17% [6, 11]. However postoperative stiffness is a relatively common complication. Overall, we observed a higher recurrence rate. The recurrence was highest in patients with diffuse disease who were treated with anterior arthroscopic surgery. Thus, addressing the posterior disease in diffuse PVNS is important to improve disease free survival. In our series, arthroscopic surgery demonstrated better success in localized disease than in diffuse disease, as reported in the literature [1, 9, 15–17, 25]. There is a paucity of literature on combined open and arthroscopic approaches [21]. We include eight patients, who were treated with anterior arthroscopic and open posterior synovectomy. Two patients had relapses for which we performed salvage surgery. The RFS was better with open anterior and posterior synovectomy compared to other approaches. This could be due to improved accessibility to posterior and extraarticular disease. As previously reported [9, 17], we found that addressing posterior disease along with anterior arthroscopic synovectomy can improve the

Table 2. Literature review

Author	Number of patients	Treatment	Average followup	Recurrences
Beguin et al. [1] 1989	13; 8 LPVNS, 5 DPVNS	Surgical synovectomy	4.2 yrs.	4
Moskovich and Parisien [16] 1991	9 LPVNS	Arthroscopic synovectomy	48 months	0
Ogilvie-Harris et al. [17] 1992	25; 5 LPVNS, 20 DPVNS	Arthroscopic synovectomy	4.6 yrs.	6
Flandry et al. [11] 1994	25 DPVNS	Open Surgical synovectomy	58 months	2
Zvijac et al. [25] 1999	14; 2 LPVNS, 12 DPVNS	Arthroscopic synovectomy	42 months	2
Kim et al. [15] 2000	11 LPVNS	Arthroscopic synovectomy	29.9 months	0
Blanco et al. [3] 2001	22	Anterior arthroscopic synovectomy + Radiation Therapy	33 months	3
Shabat et al. [20] 2002	10 DPVNS	Open Surgical synovectomy + Radiation Therapy	6 yrs.	1
Chin et al. [6] 2002	40; Recurrent DPVNS	Surgical synovectomy 10 pts; Surgery + Radiation Therapy 30 pts.	5 yrs.	7
Deponti et al. [9] 2003	19; 4 LPVNS, 15 DPVNS	Arthroscopic synovectomy	60 months	4
Ward et al. [22] 2007	9 DPVNS	Surgical synovectomy + Radiation Therapy	38 months	1
Sharma and Cheng (current study) 2009	49	18 patients: Anterior arthroscopic Partial synovectomy.	6.2 yrs.	14
	37 DPVNS	8 patients: Anterior arthroscopy + open posterior synovectomy.		2
	12 LPVNS	23 patients: Open total synovectomy (anterior + posterior approach)		5

RFS in diffuse PVNS. More extensile approaches are now being adopted in an attempt to improve the surgical excision. Flandry et al. [11] described their open technique involving multiple approaches. They only had two recurrences in 23 patients with an average followup of 58 months. Chin et al. [6] also reported their results using an extensile open posterior approach, which includes a lateral and a medial arthrotomy combined with an anterior arthrotomy. There were seven recurrences in 40 patients (18%). They used radiation therapy in most of their patients. Complications such as stiffness, contractures, and reflex sympathetic dystrophy were noted more frequently for open procedures.

Relapsed and recurrent PVNS has been a difficult problem to treat. The use of adjuvant radiotherapy along with extensile open synovectomies reportedly improves the RFS [18]. However, the use of radiation is not without complications [20, 23]. In our study we tried to study the RFS after reexcision of relapsed disease without adjuvant radiation. We found that reexcision can salvage relapses as successfully as the index surgery; however, the surgical procedure of open combined anterior and posterior synovectomy can be challenging and morbidity is associated with additional surgeries. The smaller number of patients in the salvage surgery group and the lack of comparison of clinical outcomes could be the inherent weaknesses of this comparison between the salvage and the index surgical procedures.

The success of the two procedures was however, comparable in terms of local recurrence of the disease.

We found two factors associated with higher recurrence rate are diffuse disease and arthroscopic partial synovectomy. Diffuse PVNS is more common and has a higher recurrence rate compared to the nodular type [12]. Arthroscopic partial synovectomy for diffuse PVNS of the knee is associated with higher recurrence rate [9, 17].

The goals of treatment are surgical removal of all gross disease ensuring longer RFS and reduced joint destruction. In summary, we found recurrence was frequent after synovectomy for PVNS. Complete synovectomy with anterior and posterior approach has the lowest recurrence rate for diffuse disease. Reexcision can salvage relapses; however, higher surgical morbidity may be associated with another operation. The primary factors associated with higher recurrence are diffuse disease type and subtotal arthroscopic synovectomy.

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References

1. Beguin J, Locker B, Vielpeau C, Souquieres G. Pigmented villonodular synovitis of the knee: Results from 13 cases. *Arthroscopy*. 1989;5:62–64.

2. Bertoni F, Unni KK, Beabout JW, Sim FH. Malignant giant cell tumor of the tendon sheaths and joints (malignant pigmented villonodular synovitis). *Am J Surg Pathol*. 1997;21:153–163.
3. Blanco CE, Leon HO, Guthrie TB. Combined partial arthroscopic synovectomy and radiation therapy for diffuse pigmented villonodular synovitis of the knee. *Arthroscopy*. 2001;17:527–531.
4. Byers PD, Cotton RE, Deacon OW, Lowy M, Newman PH, Sissons HA, Thomson AD. The diagnosis and treatment of pigmented villonodular synovitis. *J Bone Joint Surg Br*. 1968;50:290–305.
5. Chiari C, Pirich C, Brannath W, Kotz R, Trieb K. What affects the recurrence and clinical outcome of pigmented villonodular synovitis? *Clin Orthop Relat Res*. 2006;450:172–178.
6. Chin KR, Barr SJ, Winalski C, Zurakowski D, Brick GW. Treatment of advanced primary and recurrent diffuse pigmented villonodular synovitis of the knee. *J Bone Joint Surg Am*. 2002;84:2192–2202.
7. Chin KR, Brick GW. Extraarticular pigmented villonodular synovitis: A cause for failed knee arthroscopy. *Clin Orthop Relat Res*. 2002;404:330–338.
8. Cox D. The analysis of exponentially distributed life-times with two types of failures. *J R Stat Soc*. 1959;Series B21:411–421.
9. De Ponti A, Sansone V, Malchere M. Result of arthroscopic treatment of pigmented villonodular synovitis of the knee. *Arthroscopy*. 2003;19:602–607.
10. Flandry FC, Hughston JC. Pigmented villonodular synovitis. *J Bone Joint Surg Am*. 1987;69:942–949.
11. 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.
12. Granowitz SP, D'Antonio J, Mankin HL. The pathogenesis and long-term end results of pigmented villonodular synovitis. *Clin Orthop Relat Res*. 1976;114:335–351.
13. Jaffe HL, Lichtenstein L, Sutro CJ. Pigmented villonodular synovitis, bursitis and tenosynovitis: A discussion of the synovial and bursal equivalents of the tenosynovial lesion commonly denoted as xanthoma, xanthogranuloma, giant cell tumor or myeloplaxoma of tendon sheath with some consideration of this tendon sheath lesion itself. *Arch Pathol*. 1941;31:731–765.
14. Kaplan EL, and Meier P. Nonparametric estimation for incomplete observations. *J Am Stat Assoc*. 1958;53:457–481.
15. Kim SJ, Shin SJ, Choi NH, Choo ET. Arthroscopic treatment for localized pigmented villonodular synovitis of the knee. *Clin Orthop Relat Res*. 2000;379:224–230.
16. Moskovich R, Parisien JS. Localized pigmented villonodular synovitis of the knee: Arthroscopic treatment. *Clin Orthop Relat Res*. 1991;271:218–224.
17. Ogilvie-Harris DJ, McLean J, Zarnett ME. Pigmented villonodular synovitis of the knee. The results of total arthroscopic synovectomy, partial arthroscopic synovectomy, and arthroscopic local excision. *J Bone Joint Surg Am*. 1992;74:119–123.
18. O'Sullivan B, Cummings B, Catton C, Bell R, Davis A, Fornasier V, Goldberg R. Outcome following radiation treatment for high-risk pigmented villonodular synovitis. *Int J Radiat Oncol Biol Phys*. 1995;32:777–786.
19. Schwartz HS, Unni KK, Pritchard DJ. Pigmented villonodular synovitis. A retrospective review of affected large joints. *Clin Orthop Relat Res*. 1989;247:243–255.
20. Shabat S, Kollender Y, Merimsky O, Isakov J, Flusser G, Nyska M, Meller I. The use of surgery and yttrium-90 in the management of extensive and diffuse pigmented villonodular synovitis of large joints. *Rheumatology (Oxford)* 2002;41:1113–1118.
21. Tyler WK, Vidal AF, Williams RJ, Healey JH (2006) Pigmented villonodular synovitis. *J Am Acad Orthop Surg* 14:376–385.
22. Ward WG Sr, Boles CA, Ball J, Cline MT. Diffuse pigmented villonodular synovitis: preliminary results with intralesional resection and p32 synoviorthesis. *Clin Orthop Relat Res*. 2007;454:186–191.
23. Wiss DA. Recurrent villonodular synovitis of the knee: Successful treatment with Yttrium-90. *Clin Orthop Relat Res*. 1982;169:139–144.
24. Wu CC, Pritsch T, Bickels J, Wiernberg T, Malawar MM. Two incision synovectomy and radiation treatment for diffuse pigmented villonodular synovitis of the knee with extra-articular component. *Knee*. 2007;14:99–106.
25. Zvijac JE, Lau AC, Hechtman KS, Uribe JW, Tjin-A-Tsoi EW. Arthroscopic treatment of pigmented villonodular synovitis of the knee. *Arthroscopy*. 1999;15:613–617.