Hong Kong J Radiol. 2025;28:Epub. Published 9 December 2025 | https://doi.org/10.12809/hkjr2417948

ORIGINAL ARTICLE

Clinical and Imaging Outcomes of Radiosynoviorthesis in Haemophilic Arthropathy

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ABSTRACT

Introduction: *Radiosynoviorthesis, the intra-articular injection of radionuclides, is an established treatment for haemophilic arthropathy. This study aimed to examine the clinical and imaging outcomes of radiosynoviorthesis in Hong Kong.*

Methods: *A retrospective review of the radiosynoviorthesis cases performed from 2014 to 2023 in our tertiary referral centre was conducted. Patients' demographics, involved joints, injected radionuclides, technical success, complications, and clinical outcomes (symptoms and frequency of bleeding) were assessed.*

Results: *Radiosynoviorthesis was performed on 47 joints (22 knees, 14 elbows, 8 ankles, 2 hips, and 1 shoulder) in 26 patients. Joint injections were performed under fluoroscopic or ultrasound guidance, with a technical success rate of 98%. Six (13%) joints showed mild systemic absorption, and two (4%) joints developed transient radiation synovitis. No major complications were encountered. Excellent clinical outcomes were observed, with 83% of cases demonstrating symptomatic improvement and 91% showing a reduction in bleeding frequency. The mean monthly bleeding frequency decreased from 2.2 episodes before the procedure to 0.6 episode afterwards (p = 0.005). The total number of hospitalisations or outpatient clinic visits due to haemarthrosis decreased from 60 to 31 in the year following the procedure (p = 0.01).*

Conclusion: *Our case series suggests that radiosynoviorthesis is a safe and effective procedure that can improve clinical symptoms and reduce bleeding frequency in haemophilic arthropathy. It should be considered as part of a multidisciplinary management approach.*

Key Words: *Hemarthrosis; Hemophilia A; Injections; Knee; Radiotherapy*

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Submitted: 12 December 2024; Accepted: 9 May 2025. This version may differ from the final version when published in an issue.

Contributors: KHC and KCL designed the study. All authors acquired and analysed the data. KHC, FYW and LX drafted the manuscript. FYW, LX, TWYC, IWCW, CPL, JSML, MKC and KCL critically revised the manuscript for important intellectual content. All authors had full access to the data, contributed to the study, approved the final version for publication, and take responsibility for its accuracy and integrity.

Conflicts of Interest: All authors have disclosed no conflicts of interest.

Funding/Support: This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Data Availability: All data generated or analysed during the present study are available from the corresponding author on reasonable request.

Ethics Approval: This research was approved by the Central Institutional Review Board of Hospital Authority, Hong Kong (Ref No.: CIRB-2024-113-1). A waiver of informed consent was obtained from the Board due to the retrospective nature of the study, with strict protections in place to ensure patient privacy and the anonymity of personal data.

中文摘要

血友病性關節病放射性滑膜切除術的臨床和影像學結果

朱僑栩、尹芳盈、徐璐、錢永恩、黃偉宗、林靖邦、劉詩敏、陳文光、黎國忠

引言：放射性滑膜切除術，即關節內注射放射性核素，是治療血友病性關節病的成熟方法。本研究旨在探討放射性滑膜切除術在香港的臨床與影像學成效。

方法：本研究回顧分析了本中心於2014年至2023年間進行的放射性滑膜切除術病例。評估內容包括患者的人口學特徵、受累關節、注射的放射性核素種類、技術成功率、併發症，以及臨床療效（症狀及出血頻率）。

結果：共為26位患者的47個關節（包括22個膝關節、14個肘關節、8個踝關節、2個髖關節及1個肩關節）進行放射性滑膜切除術。關節注射在透視或超聲影像引導下進行，技術成功率達98%。其中6個關節（13%）出現輕微的全身性放射性物質吸收，2個關節（4%）出現短暫性放射性滑膜炎，未見重大併發症。臨床效果理想，83%的病例症狀有所改善，91%的病例出血頻率下降。平均每月出血次數由術前的2.2次顯著下降至術後的0.6次（$p = 0.005$）。術後一年內，因關節積血而導致的住院及門診就診總次數由60次減少至31次（$p = 0.01$）。

結論：本病例系列顯示，放射性滑膜切除術是一項安全且有效的治療方式，能改善血友病性關節病患者的臨床症狀並降低出血頻率，應納入多學科綜合治療方案中。

INTRODUCTION

Patients with haemophilia and von Willebrand disease show an increased tendency to bleed. These patients can present with recurrent haemarthrosis.[1] The synovium becomes hypertrophied due to the inflammatory response to iron deposition within the joint.[2] Increased vascularity in the inflamed synovium renders it more prone to bleeding. This creates a vicious cycle, leading to cartilage and bone damage and resulting in arthropathy.

Prevention and treatment of musculoskeletal damage are paramount in the care of patients with bleeding disorders. Prophylactic measures include coagulation factor replacement therapy and subcutaneous emicizumab injections to reduce bleeding and prevent subsequent haemarthropathy.[3] These measures have provided greater protection for patients and significantly improved patients' quality of life. However, recurrent haemarthrosis remains an issue for some patients despite advances in medical treatments.[3] In the past, surgical synovectomy was employed in patients who failed to respond to medical treatment.[4] Over time, more studies have reported favourable clinical outcomes with non-surgical synovectomy, which includes intra-articular injection of radioisotopes (radiosynoviorthesis) or antibiotics such as rifampicin.[1,5-7] These minimally invasive interventions have gained popularity and are now considered viable alternatives to surgery.[8,9] Surgery is reserved for cases when intra-articular injections are unsuccessful.

Radiosynoviorthesis, also referred to radiation synovectomy, involves the injection of radionuclides into affected joints, leading to fibrosis of the inflamed and hypertrophied synovium.[10] The primary objectives of this treatment are to reduce bleeding frequency and alleviate clinical symptoms such as pain and swelling. Once absorbed by the synovium, the radionuclides emit high-energy beta particles that induce cell death and obliterate the capillary blood supply.[11] This results in fibrosis and sclerosis of the synovial membrane, as well as a significant decrease in inflammatory activity and angiogenesis, ultimately reducing the bleeding tendency.

Although international guidelines and studies are available for Western populations, there remains a limited focus on Asian haemophilic patients and our local population.[12,13] In this retrospective study, we aimed to evaluate the technical success, efficacy, and safety of radiosynoviorthesis in our tertiary referral centre in Hong Kong.

METHODS

All cases of radiosynoviorthesis performed on patients with haemophilic arthropathy in Queen Elizabeth Hospital between 2014 and 2023 were retrospectively reviewed. Data were collected on patient demographics, type of bleeding disorder, joints treated, radionuclides administered, technical success, clinical outcomes, and complications.

Technical success was defined as successful joint puncture and intra-articular injection of radionuclides, confirmed by postprocedural scintigraphy. Clinical outcomes were assessed by evaluating patient records for changes in joint pain, swelling, and bleeding frequency. As transient synovitis could cause temporary symptoms following the procedure, patients' symptoms were evaluated at least 3 months afterwards. Clinical assessments were performed during follow-up visits 6 to 12 months post procedure. Bleeding frequency was compared by analysing the monthly bleeding episodes before the procedure and 12 months after the procedure. The number of hospitalisations or outpatient clinic appointments due to haemarthrosis during the same period was also recorded. Comparisons were analysed using the Wilcoxon signed-rank test.

Techniques

Patients with disturbing pain and recurrent haemarthrosis (defined as three or more bleeding episodes in the same joint over 6 months) despite medical treatment, and with clinical or radiological evidence of synovitis, were considered indicated for radiosynoviorthesis and referred by haematologists.[10] Initial evaluation was conducted by nuclear medicine physicians. Contraindications included pregnancy, breastfeeding, or local skin infection at the targeted joint.[14] Relative contraindications included severe joint instability, bony destruction, or significant cartilage loss. Preprocedural imaging, including X-rays, ultrasound, and/or magnetic resonance imaging, was used to assess the severity of synovitis and arthropathy (Figure 1).

The choice of radionuclides was based on the size of the joint and required tissue penetration. Two beta-emitting isotopes were used, namely, yttrium-90 (^{90}Y) and rhenium-186 (^{186}Re).[15] These isotopes exhibit different physical characteristics. ^{90}Y, with a maximum beta energy of 2.26 MeV and a mean tissue penetration of 3.6 mm, was used for knee joint. ^{186}Re, with a maximum beta energy of 0.98 MeV and a mean penetration of 1.2 mm, was employed for medium-sized joints including the hip, shoulder, elbow, and ankle. Doses ranged from 4.4 to 5.2 mCi (162.8-192.4 MBq) of ^{90}Y for knees, 2.1 to 2.2 mCi (77.7-81.4 MBq) of ^{186}Re for ankles, and 5.3 mCi (196.1 MBq) of ^{186}Re for shoulders and hips.

All procedures were performed in ambulatory setting. Under ultrasound or fluoroscopic guidance, the joint was punctured, and contrast medium was injected to confirm intra-articular location. The radionuclide was then administered, along with a long-acting corticosteroid such as triamcinolone acetonide, to reduce the risk of radiation-induced synovitis and minimise leakage.[11] The needle tract was flushed with saline during withdrawal to prevent radiation necrosis of the puncture site.

After the procedure, the affected joint was immobilised for 48 hours using a splint to reduce the risk of leakage into surrounding tissues.[16] Bremsstrahlung imaging was employed within 24 hours to confirm intra-articular distribution of the radiopharmaceutical. Patients were counselled on hygiene precautions due to urinary excretion of the radionuclide. They were instructed to flush the toilet twice after each use, wash their hands thoroughly, avoid soiling underclothing or areas around the toilet bowl, and wash any soiled garments separately. Clinical follow-up was carried out by haematologists.

RESULTS

A total of 26 male patients, aged between 10 and 57 years (median, 35), underwent radiosynoviorthesis during the study period (Table). The mean duration of follow-up was 76 months (range, 10-116). Among them, 23 patients had haemophilia A, two had haemophilia B, and one had von Willebrand disease. A total of 47 joints were injected: 22 (47%) knees, 14 (30%) elbows, eight (17%) ankles, two (4%) hips, and one (2%) shoulder.

Technical success was achieved in 46 (98%) out of the 47 joints. In one case, the right hip joint could not be accessed due to advanced degenerative changes.

Improvement in symptoms, specifically pain and swelling, was observed in 38 (83%) joints (95% confidence interval [95% CI] = 69%-92%). Eight (17%) joints showed no change in symptoms (95% CI = 8%-31%), and no joint demonstrated worsening. Three patients experienced partial symptom relief after the first injection and subsequently underwent a second injection 6 months later, after which all reported further improvement. Although routine follow-up imaging was not conducted for every patient,

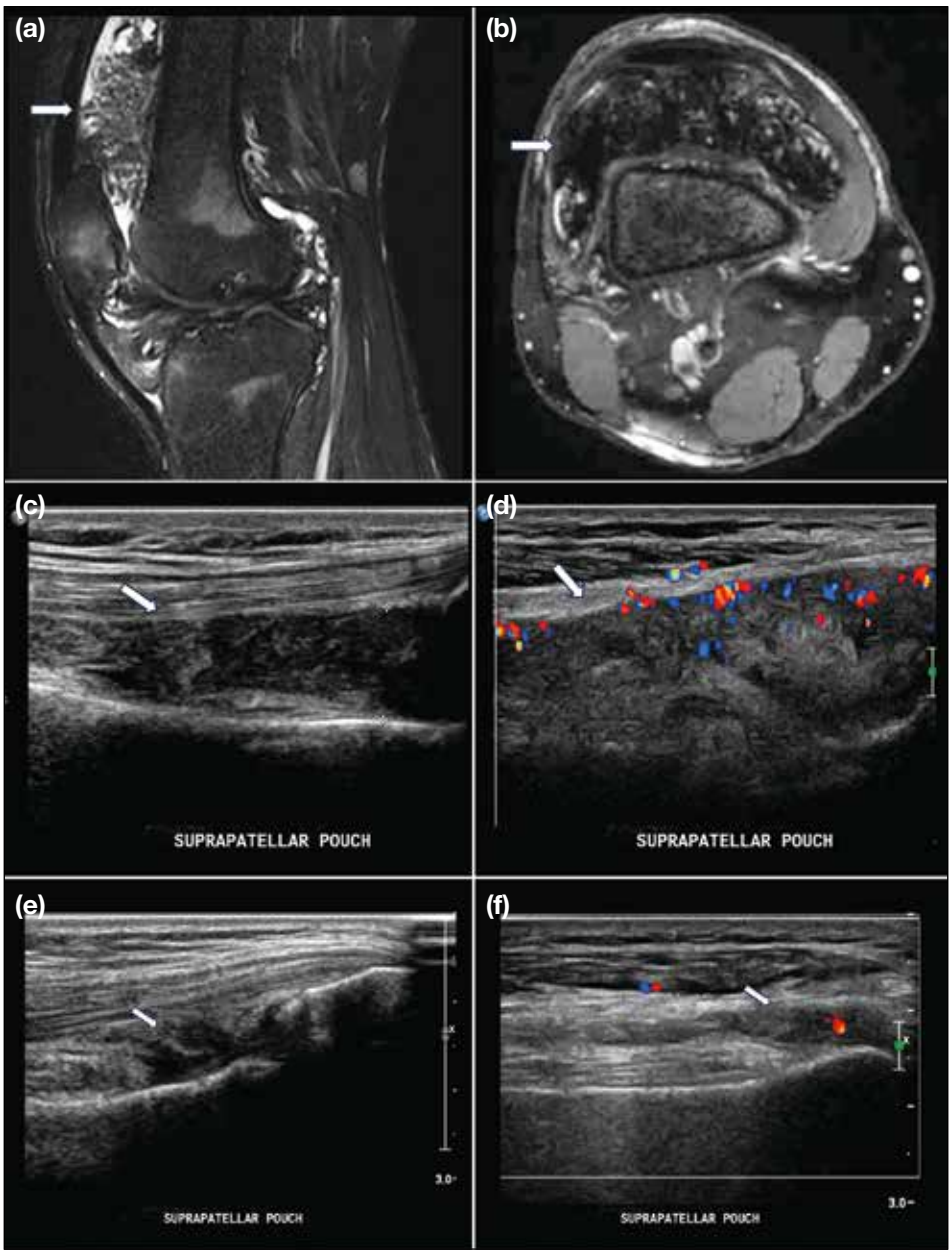

Figure 1. Preprocedural and postprocedural imaging of the left knee of a 22-year-old male with haemophilia A who had recurrent haemarthroses for 2 years despite regular factor replacement therapy. Preprocedural magnetic resonance imaging sagittal T2-weighted fat-saturated image (a) shows synovial proliferation, most severe in the suprapatellar recess (arrow). Axial T2-weighted fat-saturated image (b) shows marked susceptibility artefact (arrow), consistent with haemosiderin deposits. Preprocedural ultrasound images (c, d) show a distended suprapatellar pouch with heterogeneous soft tissue and hypervascularity (arrows), suggestive of synovitis. Four-week postprocedural ultrasound images (e) and (f) show a reduction in synovial proliferation and vascularity (arrows).

ultrasound in selected cases showed reduced synovial proliferation and vascularity, indicating improvement (Figure 1).

A reduction in bleeding frequency was noted in 42 (91%) joints (95% CI = 79%-98%), while four (9%) joints showed no change (95% CI = 2%-21%). No joint exhibited increased bleeding frequency. The mean monthly bleeding frequency decreased from 2.2 episodes (range, 0.5-6) before the procedure to 0.6 episode (range, 0-4) afterwards ($p = 0.005$). Hospitalisations and outpatient clinic visits due to haemarthrosis decreased from 60 to 31 in the year following the procedure ($p = 0.01$).

There were no major complications or procedure-related mortality. There were no documented cases of bleeding, infection, or necrosis.[17,18] Minor complications or side-effects were observed in eight cases. Six (13%) joints showed postprocedural scintigraphic uptake in the liver and spleen, suggestive of systemic absorption (95% CI = 5%-26%) [Figure 2]. Liver function tests during follow-up were normal, and these patients still experienced clinical improvement.

Two (4%) joints developed transient radiation synovitis (95% CI=0.5%-15%), characterised by pain and swelling shortly after the procedure. Ultrasound confirmed increased joint effusion and synovitis (Figure 3). These symptoms resolved within 2 weeks following conservative treatment with ice packs and nonsteroidal anti-inflammatory drugs.

DISCUSSION

This study demonstrated that most patients with bleeding disorders and recurrent haemarthrosis responded well to radiosynoviorthesis. Our findings are consistent with previous international studies. A systematic review and a meta-analysis reported an overall response rate of 72.5%.[19] Radiosynoviorthesis can be performed in paediatric patients with appropriate selection and dosage adjustment,[20] as shown by the successful treatment of a 10-year-old in our cohort. It offers the advantages of reduced hospital stays and lower costs compared with surgical synovectomy. Moreover, it can be repeated up to three times per joint, with intervals of at least 6 months.[21]

It can be difficult to perform intra-articular injection, particularly in patients with severely deformed joints. According to the literature, the best clinical improvement was identified in patients with high inflammatory activity in an early phase of arthropathy.[22] Therefore, this procedure is expected to have maximal benefit in patients in the earlier stages of arthropathy.

Radiosynoviorthesis is well tolerated, with a low incidence of side-effects or complications. Extra-articular activity was uncommon and was not accompanied by clinically significant side-effects. Direct leakage out of the joint space was rare, but systemic absorption could occur due to uptake by the lymphatic circulation and, subsequently, the bloodstream. This may be reduced by immobilisation of the joints. Patients were encouraged to increase their fluid intake and to void frequently. Two patients experienced radiation-induced synovitis in our review. It was a clinical manifestation of rapid and extensive synovial tissue necrosis that can occur 6 to 48 hours after the procedure.[23] The joint pain, swelling, and effusion are usually self-limiting and can be treated conservatively by cooling the joint with ice packs and, if

Table. Demographics and clinical characteristics of patients (n = 26) and injected joints (n = 47).*

Age, y	
<18	1 (4%)
18-25	3 (12%)
26-35	10 (38%)
>35	12 (46%)
Gender	
Male	26 (100%)
Female	0
Bleeding disorders	
Haemophilia A	23 (88%)
Haemophilia B	2 (8%)
von Willebrand disease	1 (4%)
Joints	
Knee	22 (47%)
Elbow	14 (30%)
Ankle	8 (17%)
Hip	2 (4%)
Shoulder	1 (2%)

* Data are shown as No. (%).

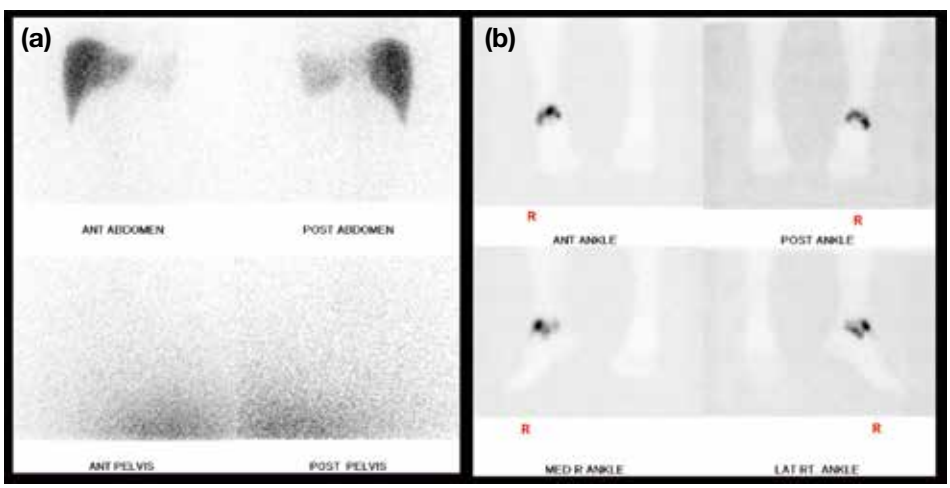

Figure 2. Scintigrams of a 24-year-old male with haemophilic arthropathy of the right ankle following radiosynoviorthesis using rhenium-186. (a) Planar images of the abdomen and pelvis show tracer activity in the liver and spleen. (b) Planar images of the ankle show tracer activity within the joint space of the right ankle, confirming the intra-articular location of the radionuclide.

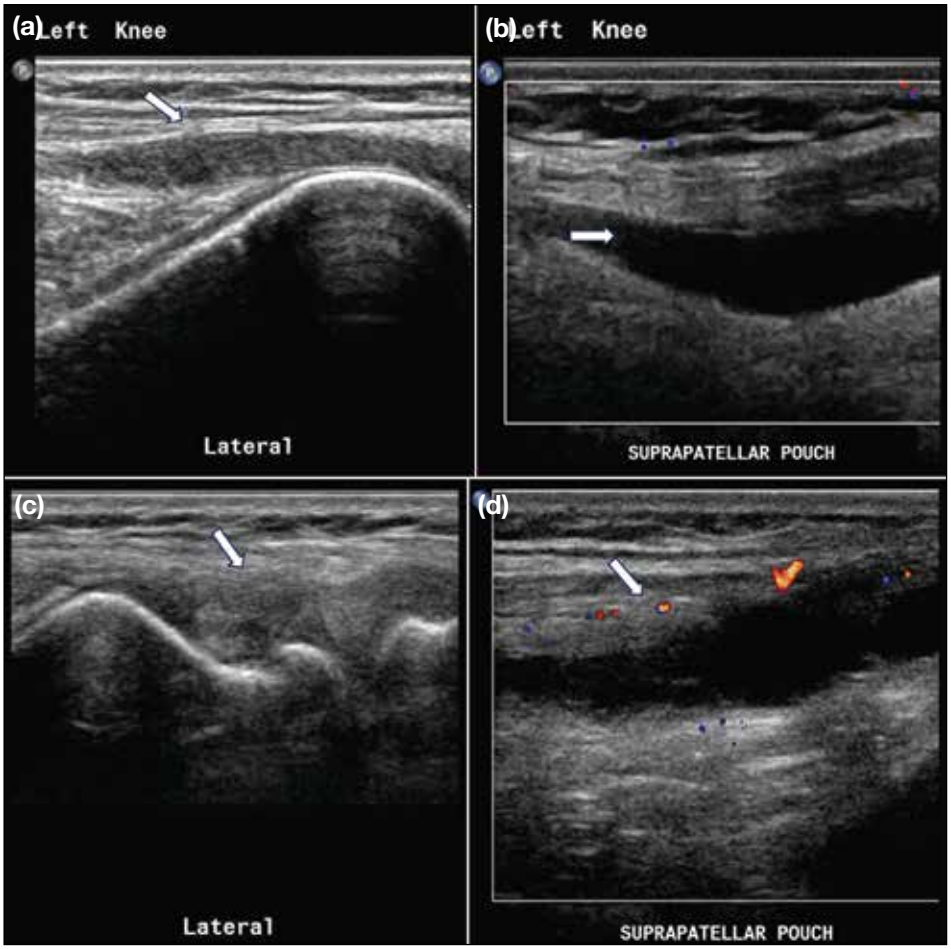

Figure 3. Ultrasound of the left knee of a 24-year-old male with haemophilic arthropathy before and after radiosynoviorthesis. (a, b) Preprocedural ultrasound images show a small joint effusion and mild synovial thickening with increased vascularity (arrows). (c, d) Postprocedural ultrasound images after 2 weeks show progression of both the joint effusion and synovial thickening (arrows). Patient's symptoms of pain and swelling have resolved within 2 weeks with conservative treatment. The features are suggestive of transient radiation synovitis.

necessary, with anti-inflammatory drugs. Intra-articular corticosteroid injection during the procedure can reduce inflammation and decrease leakage of the radioisotope through dilated capillaries of the synovium into the systemic circulation.

Limitations

There are several limitations in this study. First, it was retrospective in nature, with a relatively small cohort size, and no control arm was available for comparison. Nonetheless, this study still offered results in our local population that were in line with other studies demonstrating the efficacy and safety of radiosynoviorthesis.[5-7,10,22] Another limitation was the heterogeneous study population, with different joints involved and varying severity of arthropathy. In general, most patients still showed favourable clinical outcomes. Subgroup analysis may be considered in the future with a larger number of patients.

There was no objective pain scoring system in place to provide a quantitative assessment of clinical symptoms, nor was there a standardised magnetic resonance imaging protocol to exclude patients with severe cartilage loss or degenerative joint conditions that could contribute to pain. A prospective study would be ideal for recruiting patients and conducting assessments using an objective scoring system for symptoms and a standard follow-up protocol. Radiological investigations, such as ultrasound, can be used to assess for synovitis and serve as another objective parameter in evaluating outcomes. This approach would also facilitate longitudinal comparisons to investigate long-term efficacy and allow monitoring of disease progression. Lastly, there may be potential confounders such as the co-injection of steroid with the radionuclides. The use of steroids may have caused a period of analgesia and helped bridge the gap between the administration of the radiopharmaceutical and the onset of the effects of radiosynoviorthesis. However,

such an effect was expected to be short term and unlikely to persist beyond 3 months, when our clinical assessment was conducted.

CONCLUSION

Radiosynoviorthesis is a safe and effective procedure which can contribute to symptomatic improvement and a reduction in bleeding frequency in patients with haemophilic arthropathy. It should be considered as part of a multidisciplinary management approach.

REFERENCES

1. van Galen KP, Mauser-Bunschoten EP, Leebeek FW. Hemophilic arthropathy in patients with von Willebrand disease. Blood Rev. 2012;26:261-6.
2. Hoots WK, Rodriguez N, Boggio L, Valentino LA. Pathogenesis of haemophilic synovitis: clinical aspects. Haemophilia. 2007;13 Suppl 3:4-9.
3. Oldenburg J. Optimal treatment strategies for hemophilia: achievements and limitations of current prophylactic regimens. Blood. 2015;125:2038-44.
4. Llinás A. The role of synovectomy in the management of a target joint. Haemophilia. 2008;14 Suppl 3:177-80.
5. Querol-Giner M, Pérez-Alenda S, Aguilar Rodríguez M, Carrasco JJ, Bonanad S, Querol F. Effect of radiosynoviorthesis on the progression of arthropathy and haemarthrosis reduction in haemophilic patients. Haemophilia. 2017;23:e497-503.
6. Desaulniers M, Paquette M, Dubreuil S, Senta H, Lavallée É, Thorne JC, et al. Safety and efficacy of radiosynoviorthesis: a prospective Canadian multicenter study. J Nucl Med. 2024;65:1095-100.
7. Kavakli K, Aydoğdu S, Omay SB, Duman Y, Taner M, Capaci K, et al. Long-term evaluation of radioisotope synovectomy with yttrium 90 for chronic synovitis in Turkish haemophiliacs: Izmir experience. Haemophilia. 2006;12:28-35.
8. van Vulpen LF, Thomas S, Keny SA, Mohanty SS. Synovitis and synovectomy in haemophilia. Haemophilia. 2021;27 Suppl 3:96-102.
9. Rodriguez-Merchan EC, Wiedel JD. General principles and indications of synoviorthesis (medical synovectomy) in haemophilia. Haemophilia. 2001;7 Suppl 2:6-10.
10. Kampen WU, Boddenberg-Pätzold B, Fischer M, Gabriel M, Klett R, Konijnenberg M, et al. The EANM guideline for radiosynoviorthesis. Eur J Nucl Med Mol Imaging. 2022;49:681-708.
11. Fischer M, Mödder G. Radionuclide therapy of inflammatory joint diseases. Nucl Med Commun. 2002;23:829-31.
12. Hanley J, McKernan A, Creagh MD, Classey S, McLaughlin P, Goddard N, et al. Guidelines for the management of acute joint bleeds and chronic synovitis in haemophilia: A United Kingdom Haemophilia Centre Doctors' Organisation (UKHCDO) guideline. Haemophilia. 2017;23:511-20.
13. Srivastava A, Santagostino E, Dougall A, Kitchen S, Sutherland M, Pipe SW, et al. WFH Guidelines for the Management of Hemophilia, 3rd edition. Haemophilia. 2020;26 Suppl 6:1-158.
14. Chojnowski MM, Felis-Giemza A, Kobylecka M. Radionuclide synovectomy—essentials for rheumatologists. Reumatologia. 2016;54:108-16.
15. Knut L. Radiosynovectomy in the therapeutic management of arthritis. World J Nucl Med. 2015;14:10-5.
16. Ahmad I, Nisar H. Dosimetry perspectives in radiation synovectomy. Phys Med. 2018;47:64-72.
17. Kampen WU, Matis E, Czech N, Soti Z, Gratz S, Henze E. Serious complications after radiosynoviorthesis. Survey on frequency and treatment modalities. Nuklearmedizin. 2006;45:262-8.
18. Infante-Rivard C, Rivard GE, Derome F, Cusson A, Winikoff R, Chartrand R, et al. A retrospective cohort study of cancer incidence among patients treated with radiosynoviorthesis. Haemophilia. 2012;18:805-9.
19. van der Zant FM, Boer RO, Moolenburgh JD, Jahangier ZN, Bijlsma JW, Jacobs JW. Radiation synovectomy with (90)yttrium, (186)rhenium and (169)erbium: a systematic literature review with meta-analyses. Clin Exp Rheumatol. 2009;27:130-9.
20. Manco-Johnson MJ, Nuss R, Lear J, Wiedel J, Geraghty SJ, Hacker MR, et al. 32P radiosynoviorthesis in children with hemophilia. J Pediatr Hematol Oncol. 2002;24:534-9.
21. Clunie G, Fischer M; EANM. EANM procedure guidelines for radiosynovectomy. Eur J Nucl Med Mol Imaging. 2003;30:BP12-6.
22. Kresnik E, Mikosch P, Gallowitsch HJ, Jesenko R, Just H, Kogler D, et al. Clinical outcome of radiosynoviorthesis: a meta-analysis including 2190 treated joints. Nucl Med Commun. 2002;23:683-8.
23. Pirich C, Schwameis E, Bernecker P, Radauer M, Friedl M, Lang S, et al. Influence of radiation synovectomy on articular cartilage, synovial thickness and enhancement as evidenced by MRI in patients with chronic synovitis. J Nucl Med. 1999;40:1277-84.

